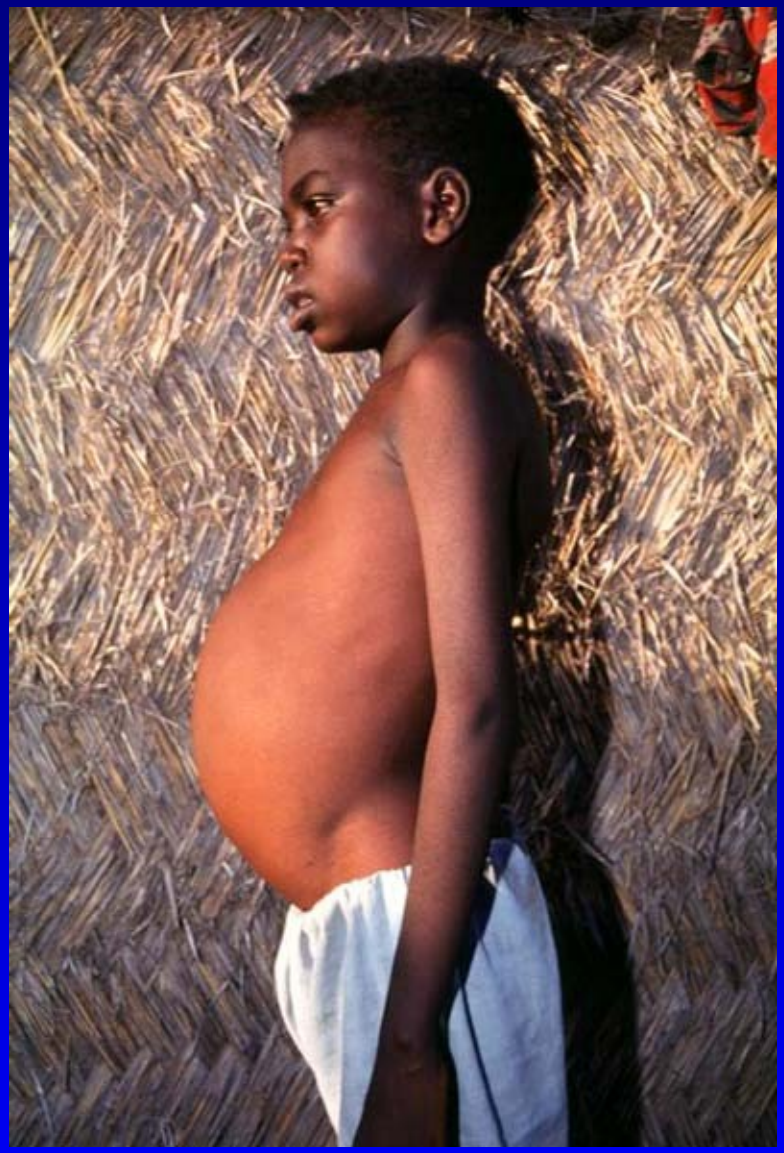

GLOBAL MEDICINE
2 - 13 February 2004

USAF Course Number:
B30ZY48X0-000

Leishmaniasis

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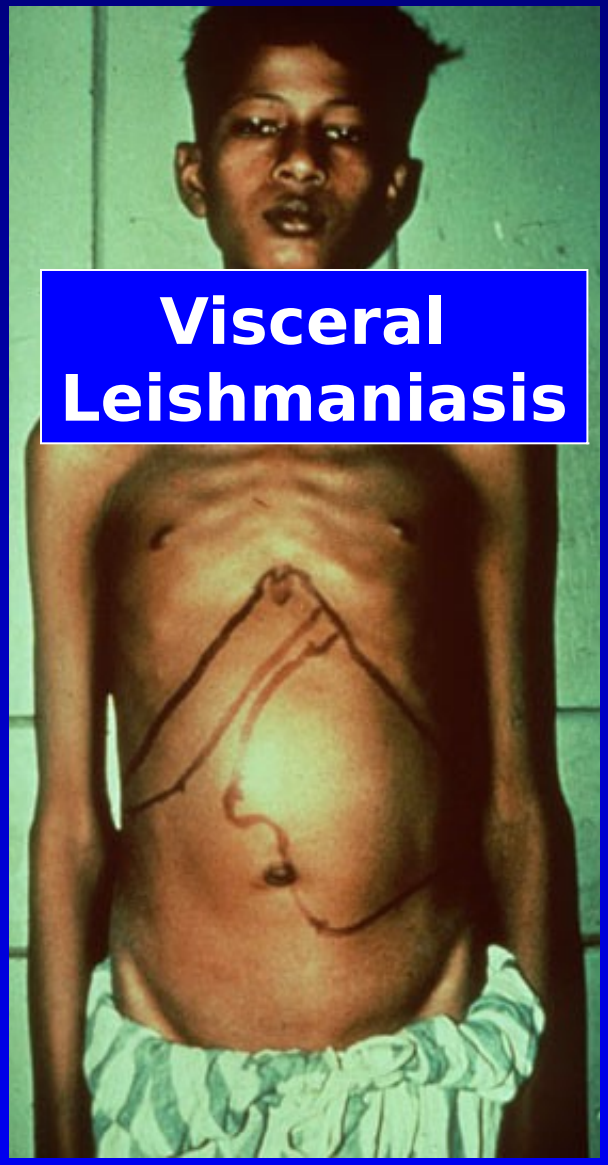
The Leishmaniases

- A diverse group of protozoan parasites
- Intracellular pathogens of the macrophage
- Different clinical manifestations / syndromes
- Zoonosis
  - Sand fly insect vector
  - Mammalian reservoir(s)
  - Man is incidental host
    - Indian VL and *L. tropica* CL are exceptions

William Leishman & Charles Donovan

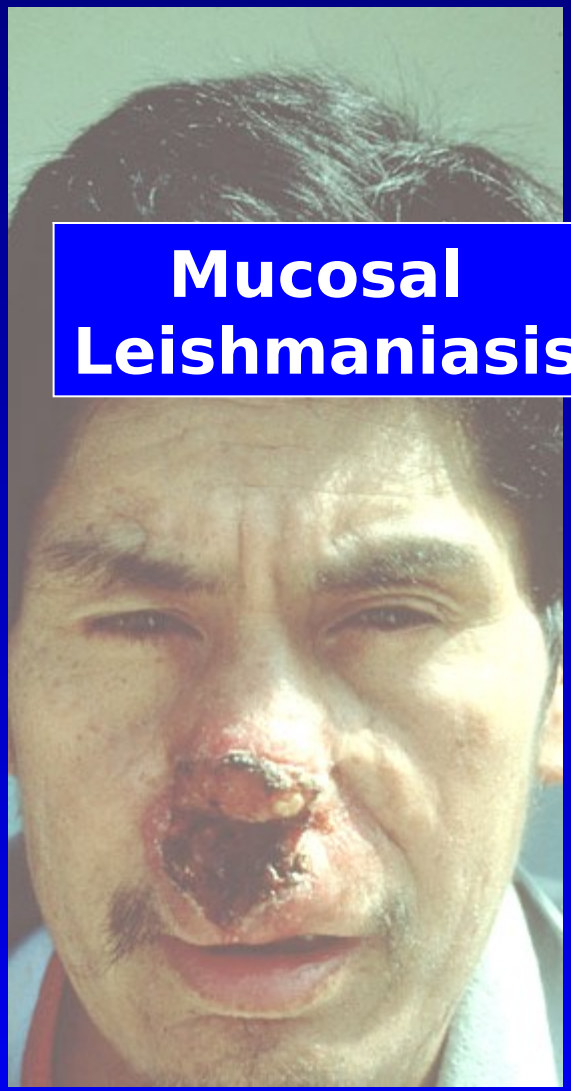
3 Major Clinical Syndromes

- Visceral leishmaniasis
- Cutaneous leishmaniasis
- Mucosal leishmaniasis



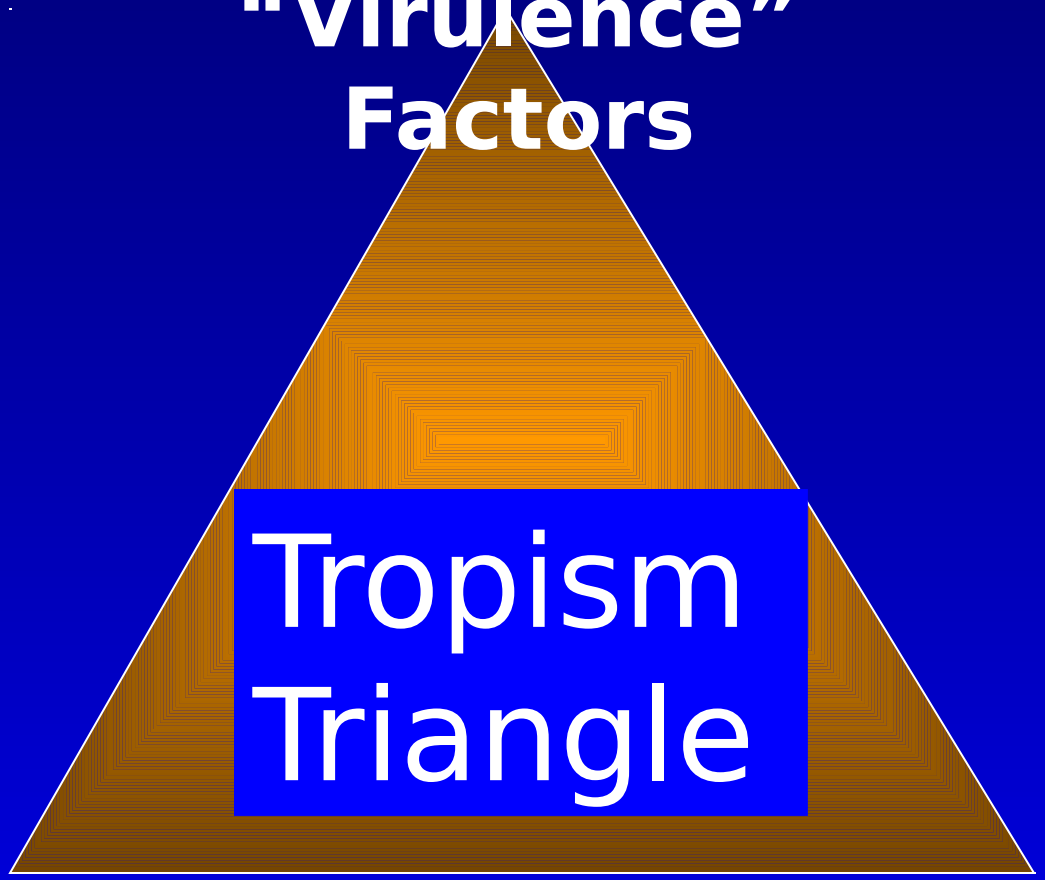
Visceral Leishmaniasis

Cutaneous Leishmaniasis



Mucosal Leishmaniasis

Parasite "Virulence" Factors

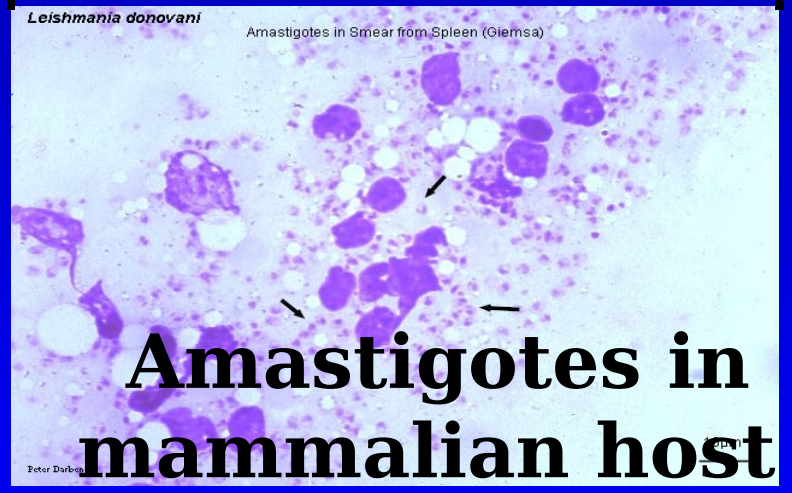


Genetic Background of the Host

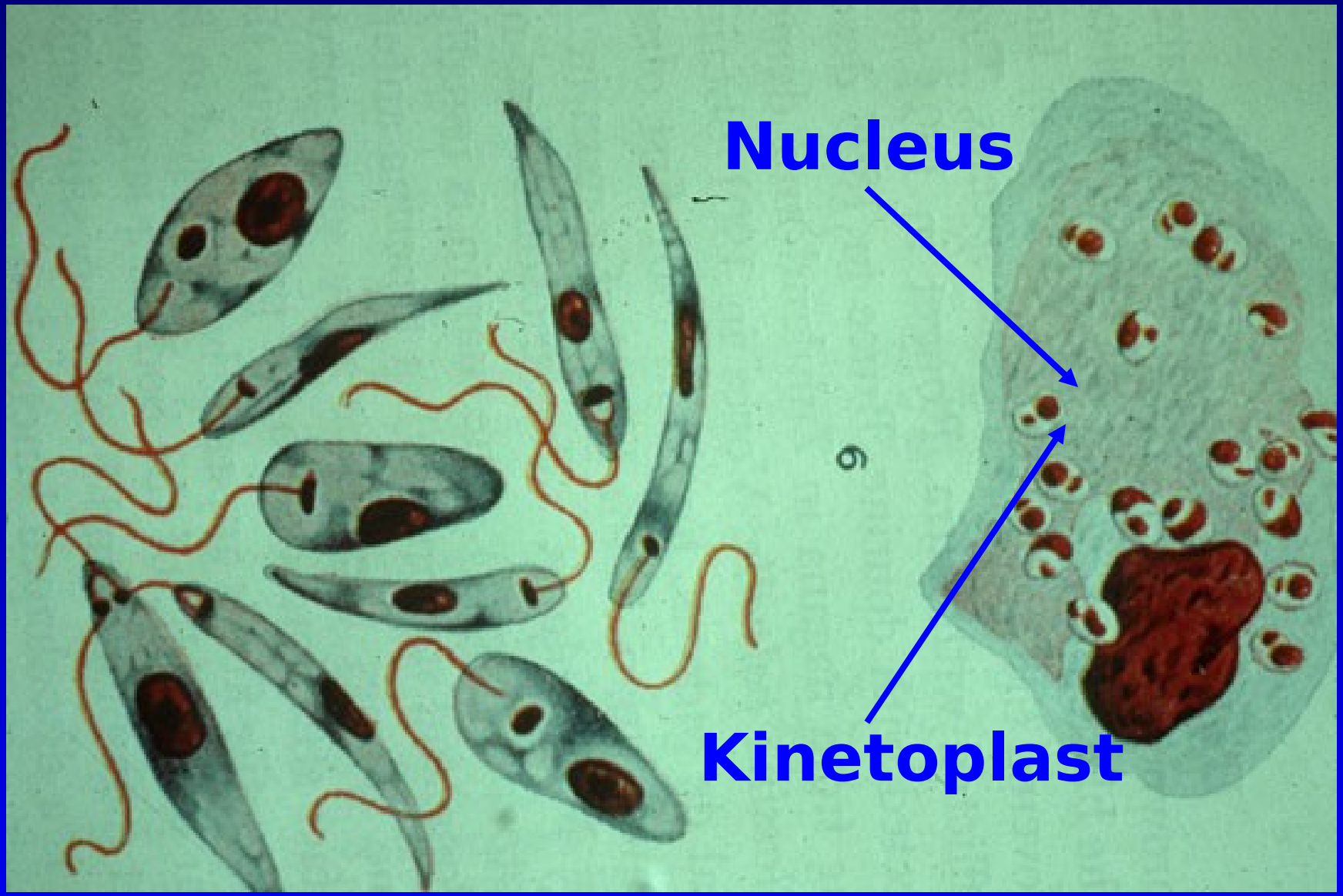
Sand Fly Salivary Factors

Parasite Life Cycle

Promastigotes in sand fly



Amastigotes in mammalian host


Nucleus
Kinetoplast

Cutaneous Syndromes

- **Cutaneous leishmaniasis**
  - **Localized, ulcerative**
  - **Nodular**
  - **Other: Psoriaform, verrucous, plaque, macules**
- **Diffuse cutaneous leishmaniasis**
- **Leishmaniasis recidivans**
- **Mucosal leishmaniasis**
- **Post Kala Azar Dermal Leishmaniasis (PKDL)**

Disease Spectrum Based on Immunological Response to Infection

Paucibacillary → **Multibacillary**

Leprosy

Oligoparasitic → **Polyparasitic**

Leishmaniasis

Classification by Parasite Burden

- Oligoparasitic **Polyparasitic**
- Cutaneous (Dermotropic) Syndromes
  - Mucosal Leishmaniasis (ML)
  - Leishmaniasis recidivans (LR)
  - Diffuse Cutaneous Leishmaniasis (DCL)
  - Localized (ulcerative / nodular) cutaneous leishmaniasis (CL)
- Systemic (Viscerotropic Syndromes)
  - VL, acute febrile, chronic, adenopathy

Cutaneous Leishmaniasis

- **Cutaneous leishmaniasis**
  - **Localized, ulcerative**
  - **Nodular**
  - **Other: Psoriaform, verrucous, plaque, macules**
- **Self healing**
- **Incubation period of days to years**
- **Slowly enlarging nodule at bite site**
- **Crust forms centrally leading to ulceration with raised margins**
- **Healing leaves a hypo-pigmented and depressed scar**
- **Characteristic but inconstant clinical differences between species**

5
6

DATE
4
3
2
1

Leishmaniasis recidivans

- **Uncommon syndrome associated with *L. tropica***
- **Persistence of few organisms despite a vigorous immune response**
- **Papules around the margin of a scar**
- **Papules ulcerate, heal,and reappear over many years**
- **Plaque, psoriaform, verrucous, and keloidal lesions also described**

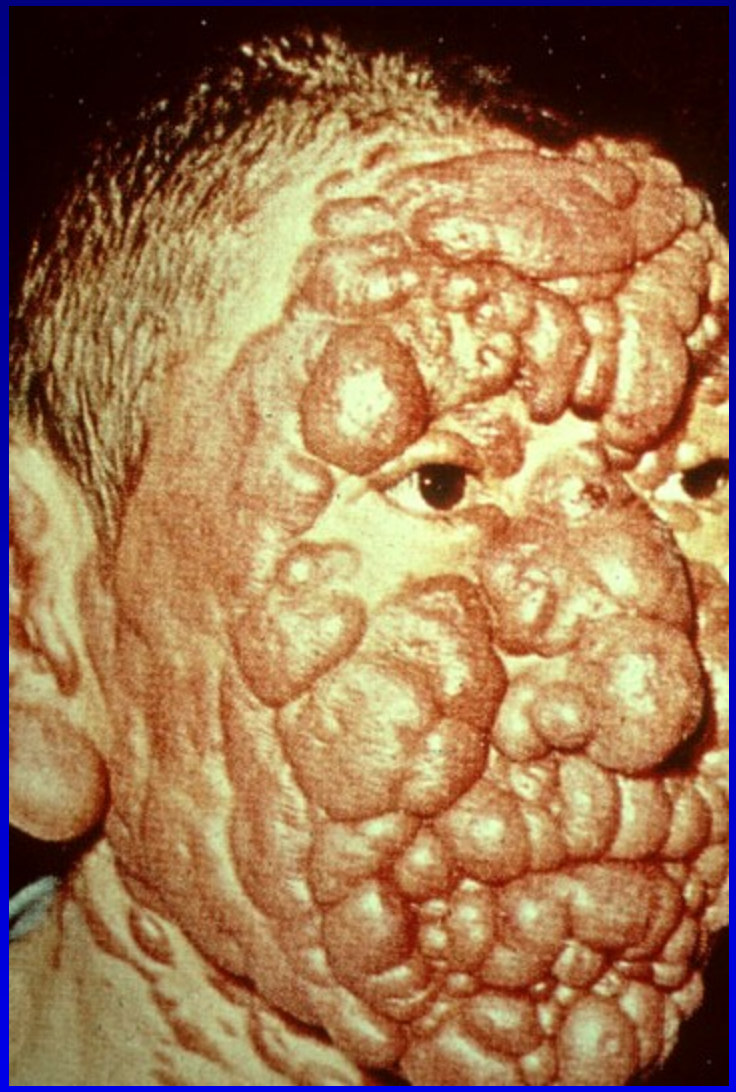
Post Kala Azar Dermal Leishmaniasis (PKDL)

- Skin papules which appear following treatment of VL with SbV in India and East Africa
- In Africa
  - More commonly seen at end of therapy in up to 50%
  - Transient crop of papules over face and forearms
  - Resolves w/o Rx over months
- In India
  - Lesions appear insidiously 1-2 years following Rx
  - Hypopigmented macules, nodules, verrucous growths, papillomatous and gigantic nodular forms
  - Slowly progressive and seldom resolve w/o Rx

Diffuse Cutaneous Leishmaniasis

- Uncommon to rare
- Chronic, progressive process over months to years
- Primary lesion does not ulcerate
- Common on face and cooler extensor surfaces of limbs
- Nodules, plaques, and hypo-pigmented macules
- May cause grotesque deformity and resembles lepromatous leprosy
- Venezuela, Ethiopia, Dominican Republic

31



Mucosal Leishmaniasis

- **“Espundia”**
- **Nodular and ulcerative lesions of the oral-nasal-pharyngeal mucosal surfaces**
- **Days to years (43!) following primary infection with *L. braziliensis***
- **Healed scar of primary CL infection usually present**
- **Nasal septum lesion or horseness often first symptom or sign**

Visceral Leishmaniasis

- *Classic "pentad"*
  - **Fever**
  - **Cachexia**
  - **Splenomegaly**
  - **Pancytopenia**
  - **Hypergamma-globulinemia**

VL Case Report: History

- 25 yo AD USAF male presents with CC of increasing difficulty completing a 2 mile run
- ROS reveals fatigue, night sweats, 30 pound weight loss over 3-4 months
- Lived in Spain from March 93 to June 94
- One visit to MD in June 94 for abrupt onset of fever, malaise
  - 5 X increase AST.
  - Resolved w/o specific dx or intervention

VL Case Report: Physical Exam and Lab

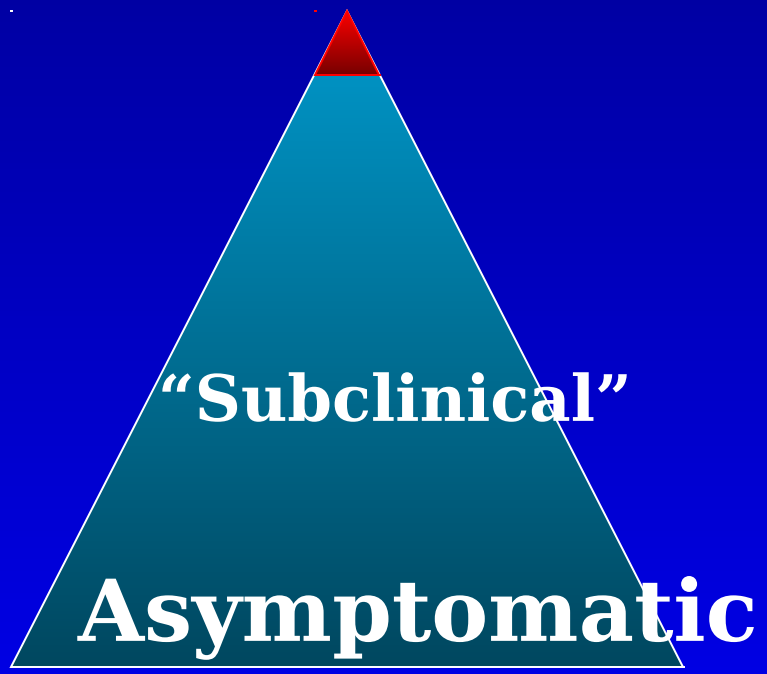
- Thin, chronically ill appearing male
- Afebrile
- Marked splenomegaly (30 cm below costal margin)
- Anemia (Hb / Hct = 7.7 / 23)
- Thrombocytopenia (WBC = 2600)
- Marked increase in total protein to 18 .4 g / dl (NR = 6.4 - 8.2 g / dl)

Clinical Presentation of VL in the Immunocompetent,Well Nourished Adult

- ***Most and Levietes. 1947. Medicine. 26:221***
  - **N=30, US military in WWII**
  - **Incubation period: 3 weeks to 33 months**
  - **Symptom onset to definitive diagnosis, mean 10 weeks (range 2 -26 weeks)**
  - **Abrupt onset of fever and chills - 96%**
  - **Splenomegaly in 90% and hepatomegaly in 73% on presentation**
  - **Parasitologic diagnosis**
    - **21 of 49 (43%) smears from bone marrow aspirations in 29 patients were (+)**
    - **8 0f 29 (28%) were not confirmed by bone marrow**
    - **18 of 18 (100%) splenic aspirates were both smear and culture positive**

Visceral Leishmaniasis Disease Spectrum

1-3% with overt VL

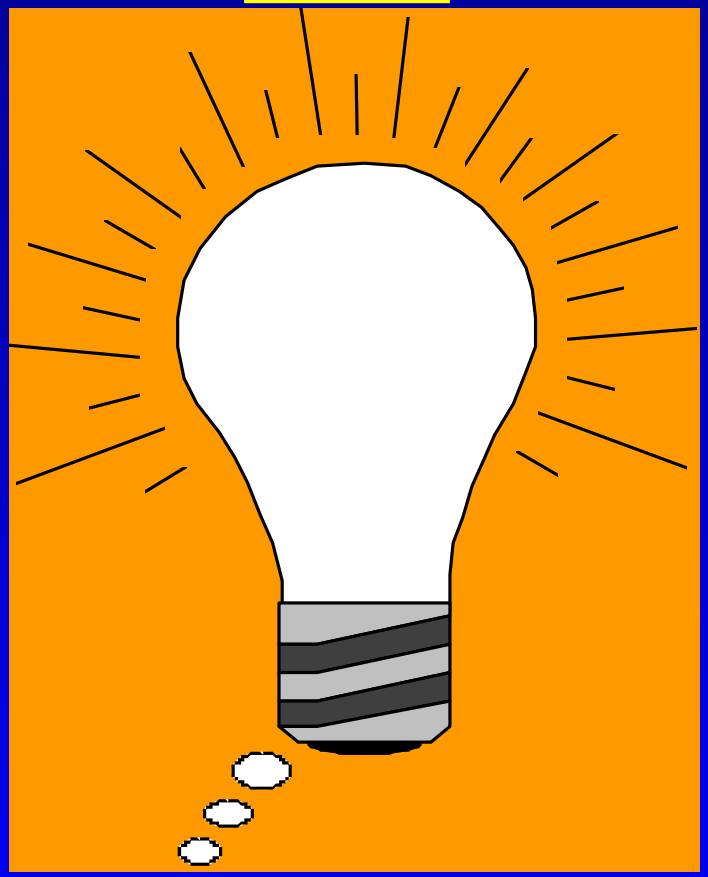


- **"Subclinical" Syndromes**
  - **Chronic systemic illness**
  - **Acute febrile illness**
- **Risk factors for progression**
  - **Malnutrition**
  - **Immunosuppression (AIDS)**
  - **Genetic?**
- **Cause of death**
  - **Measles**
  - **Pneumonia**
  - **TB**
  - **dysentery**

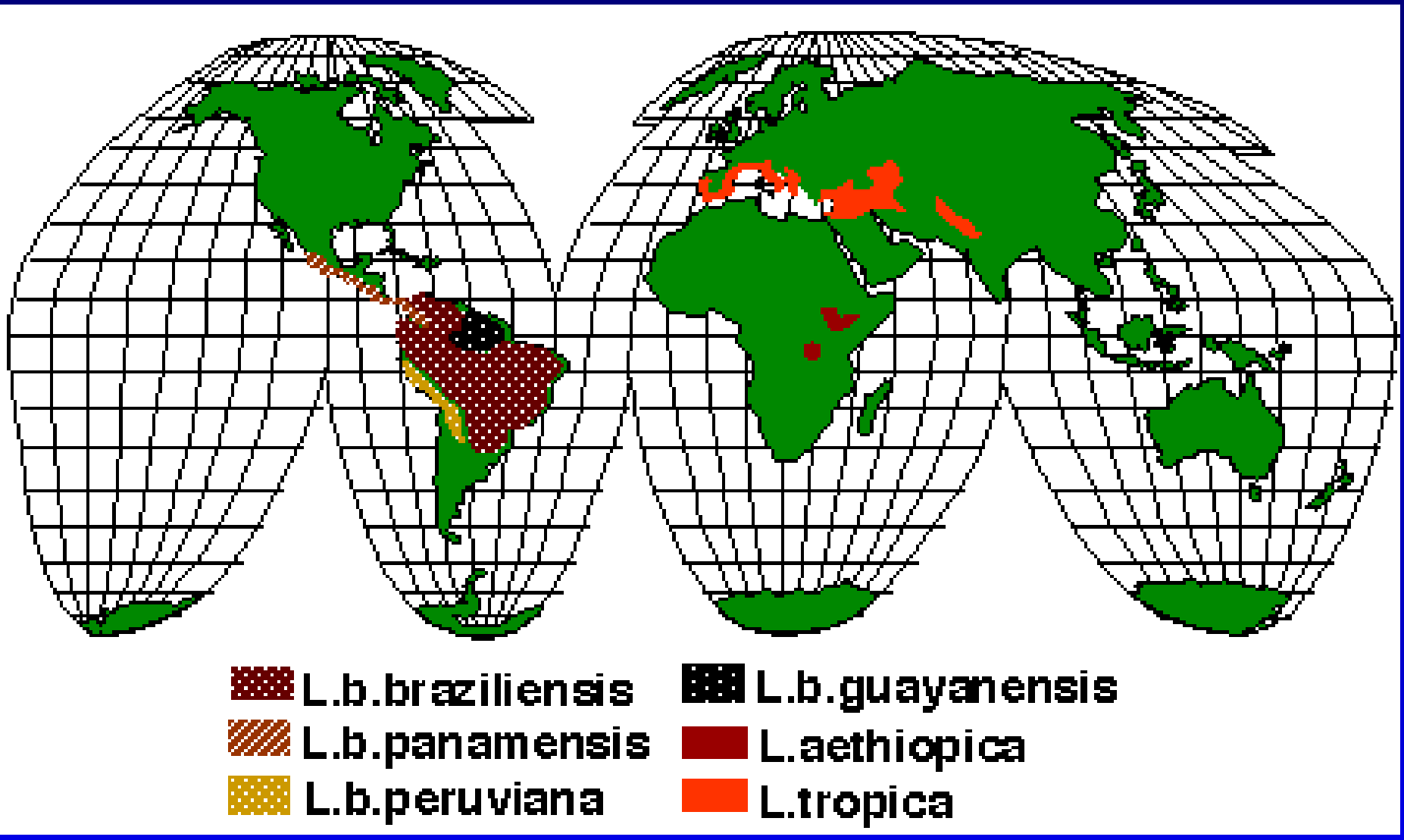
Leishmaniasis as an OI in the Immunocompromised Host

- ***Primary disease***
  - **HIV, SLE, Hodgkin's disease, acute leukemia**
- ***Immunosuppressive drugs***
  - **Cyclosporin A, prednisone, cyclophosphamide, azathioprine**
- ***Organ transplantations***
  - **Kidney, Heart, Liver**

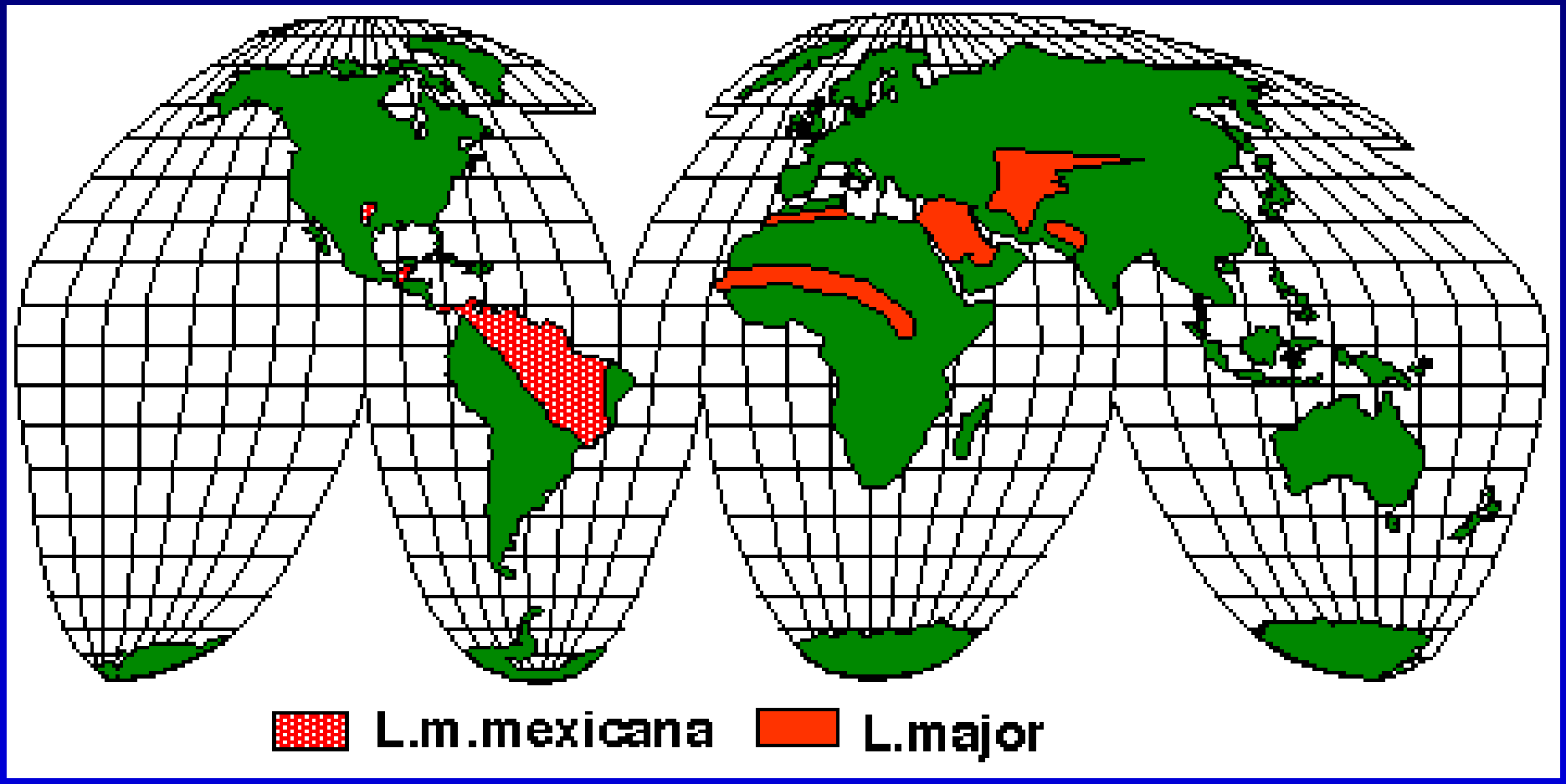
Diagnosis



- Travel history
- Deployment history
- Birth history
- Residence history
- Occupational exposure
- Blood transfusions
- Congenital



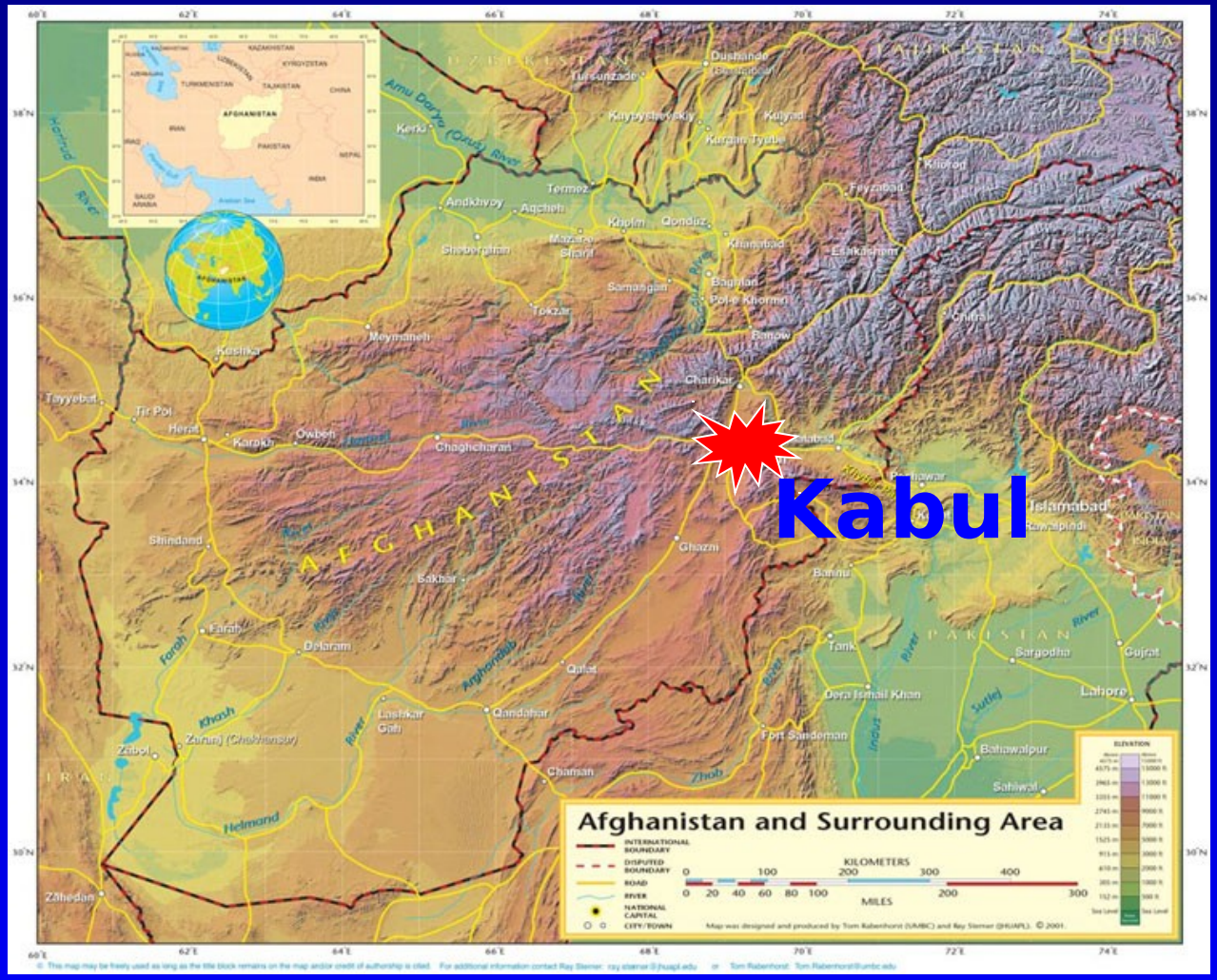
Courtesy of http://www.icp.ucl.ac.be/~opperd/parasit



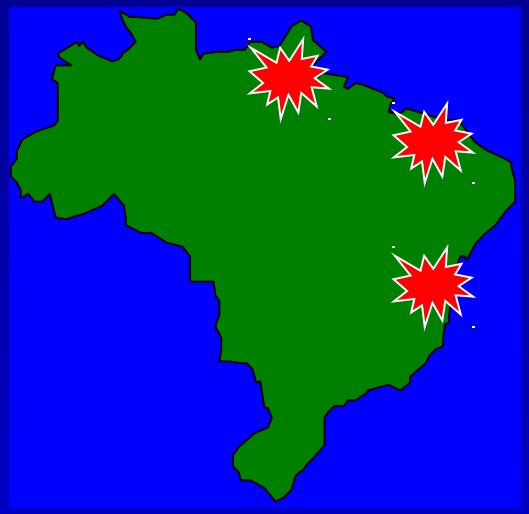
Courtesy of http://www.icp.ucl.ac.be/~opperd/parasi

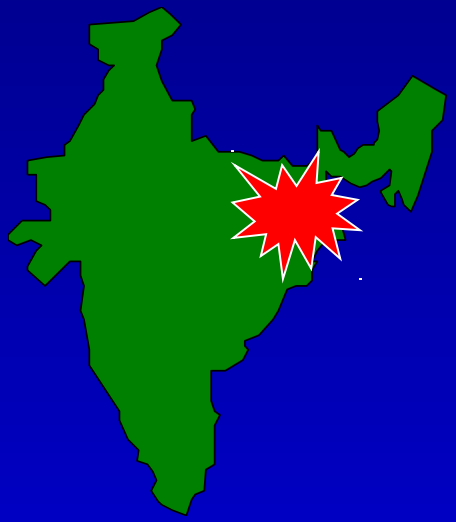
http://www.who.int/emc/diseases/leish/leisgeo1

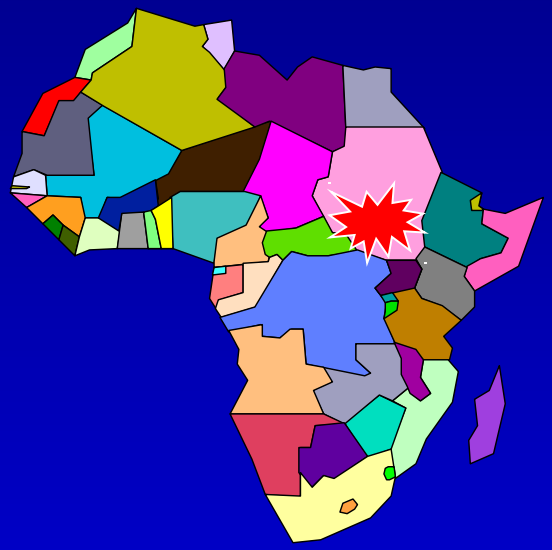
Epidemic L. tropica: 2004



Epidemic VL: 2004

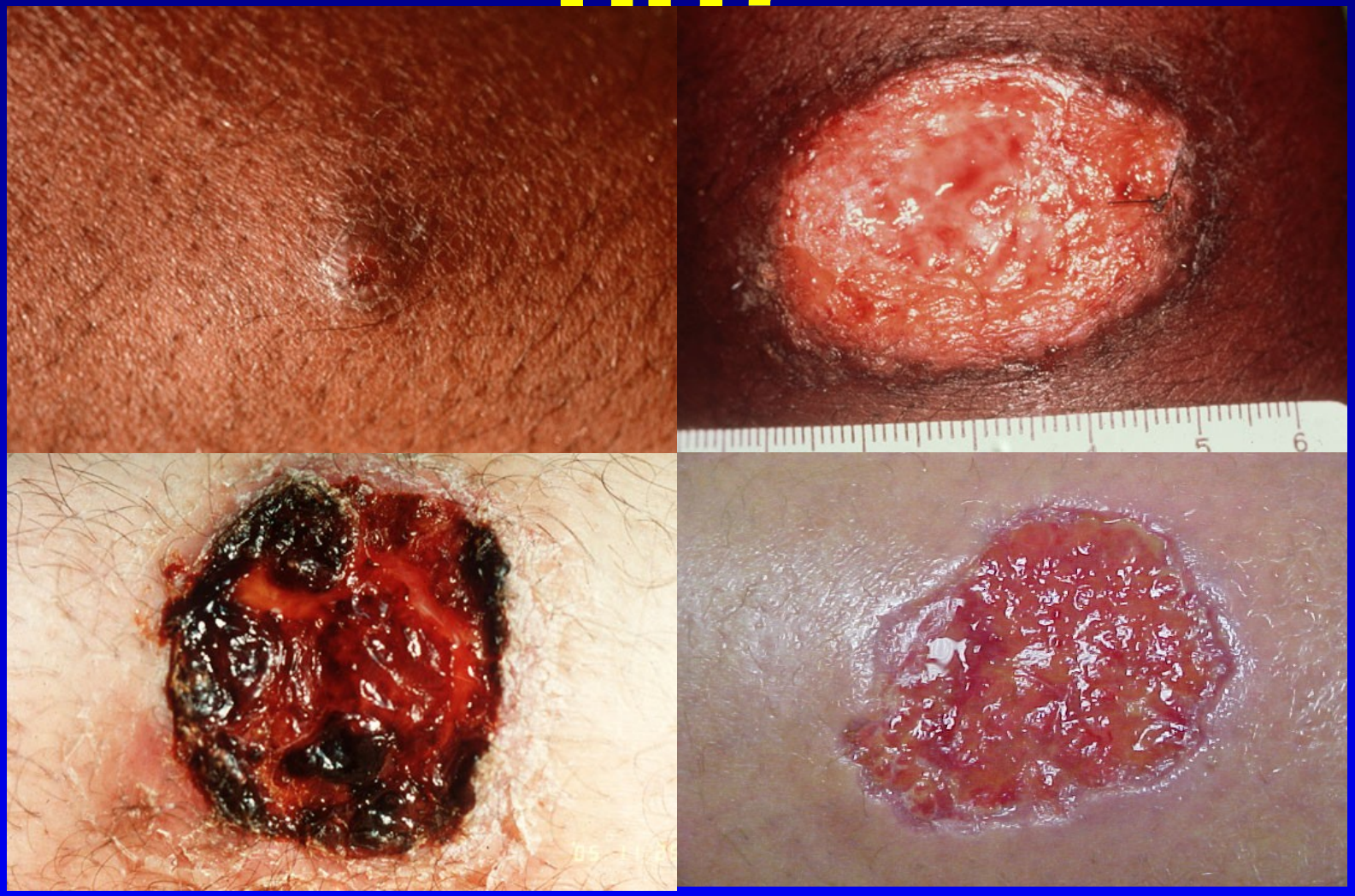






Brazil **India** **Sudan**

So now what do I do?



Diagnostic Approaches

- **Clinical / epidemiological diagnosis**
- **Parasitologic Diagnosis**
  - **Amastigotes on a slide or in tissue**
  - **Promastigotes in culture**
  - **Molecular**
- **Immunological Diagnosis**
  - **Serology**
  - **Delayed type hypersensitivity (DTH) via skin test**

Disease Spectrum Based on Immunological Response to Infection

Paucibacillary → **Multibacillary**

Leprosy

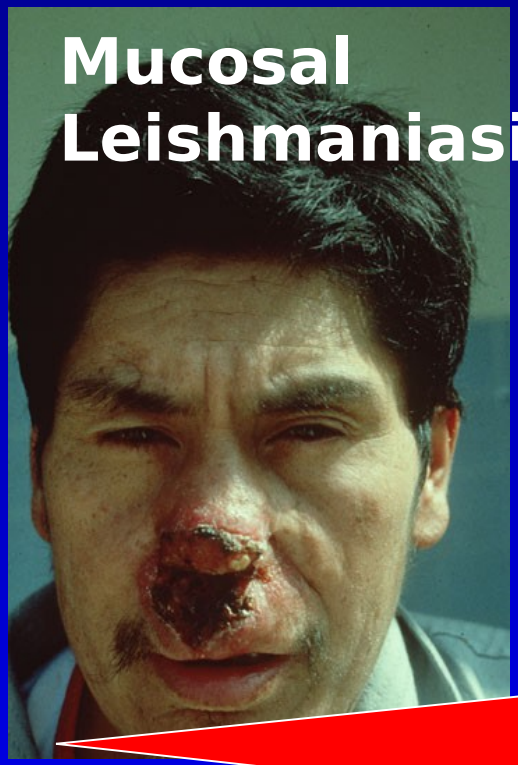
Oligoparasitic → **Polyparasitic**

Leishmaniasis

Spectrum of Disease : Diagnosis

Oligoparasitic Polyparasitic

Parasite Burden and Clinical Syndrome



Mucosal Leishmaniasis

Localized, ulcerative cutaneous leishmaniasis

Diffuse Cutaneous Leishmaniasis

Relative Parasite Burden

Parasitologic Diagnosis

- Requires invasive procedure
- Tissue specimen(s)
  - Aspirates, biopsies
  - Lesion, lymph node, bone marrow, spleen, peripheral blood
- Visualization of amastigotes
  - Giemsa stain, H&E
  - Monoclonal Abs - IFA
- Genome Detection (kDNA, genomic DNA)
  - Hybridization
  - PCR amplification

Parasite Burden in NWCL: Species

- More parasites in lesions caused by *L. mexicana* than *L. braziliensis*
  - Guatemala, N=91 L.m., N=259 L.b.
  - Amastigote concentration / 100 OIF
  - L. mexicana 100 (0-8682)
  - L. braziliensis 14 (0-13,153)
- More sensitive techniques may be needed for *L. braziliensis*

Herwaldt BL, Arana BA, Navin TR. JID 1992; 165

Parasite Burden in NWCL: Age of Ulcers

	Lesion Characteristics, median (range)	
Amastigote concentration by week	**L. mexicana N=7**	**L. braziliensis N=25**
1	**1735 (0-8682)**	**27 (0-1668)**
2	**19 (1-3545)**	**4 (0-1558)**
3	**72 (0-2564)**	**1 (0-1240)**
Lesion age (days)	**30 (15-150)**	**45 (8-180)**
Ulcer size (cm2)	**0.4 (0.04-1.3)**	**0.4 (0.09-3.8)**

Older lesions have fewer parasites !

Herwaldt BL, Arana BA, Navin TR. JID 1992; 165

Choice of Diagnostic Test?

- **Sensitivity of diagnostic test depends on parasite burden and thus clinical syndrome**

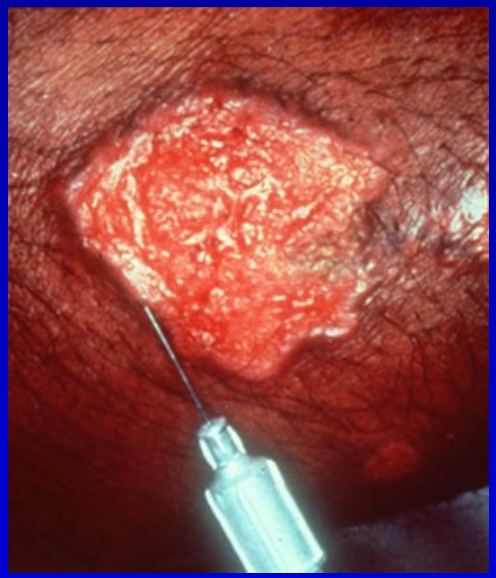
Where and how do I sample?

- Site preparation
- How to sample?
  - Scraping
  - Aspirate
  - Punch bx
- Where to sample
  - Margin versus center of ulcer

Site Preparation

- **Ulcerative lesions**
  - **Lidocaine, debridement, clean & dry ulcer base**
  - **May lightly use scrub brush**
  - **Remove all surface exudate**
- **Nodular lesions**
  - **Soap and water**
  - **± lidocaine for slit-skin**

How to get the specimens?

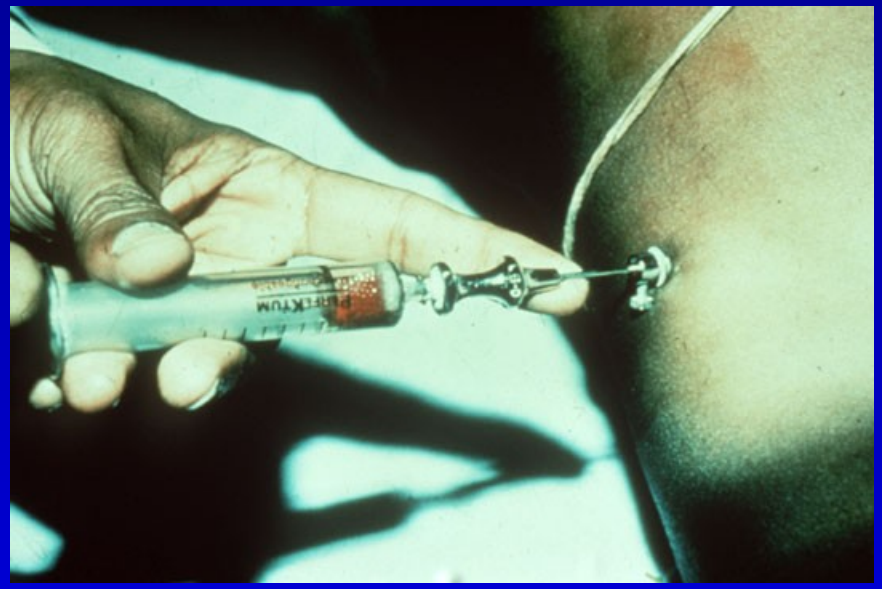


Scrape ulcer base No. 10 scalpel blade

Aspirate the lesion 2-3 mm Sterile saline in hub

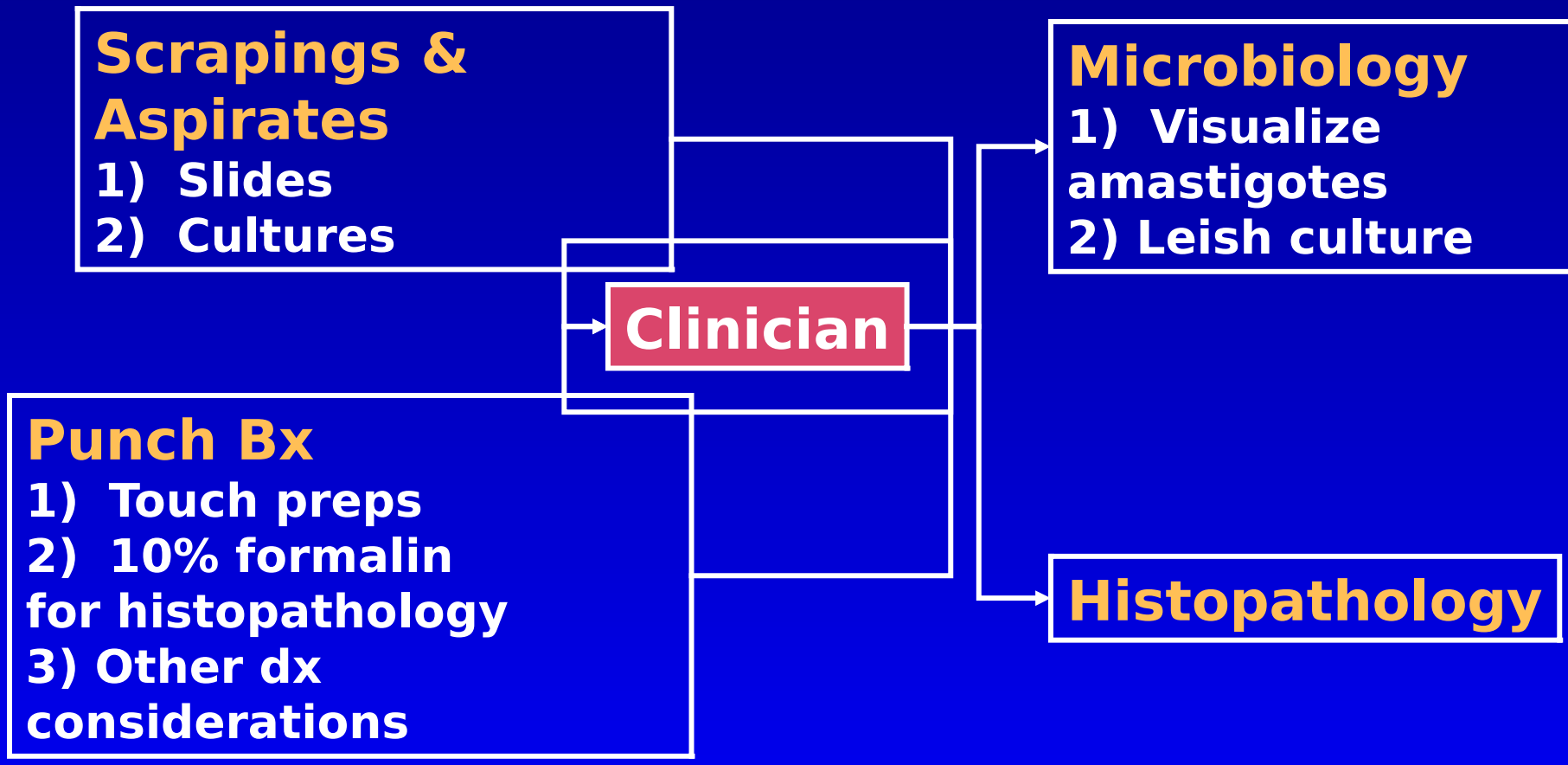
punch bx

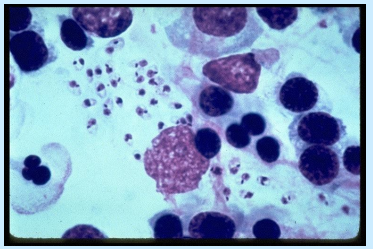
How to get the specimens?



Splenic aspiration
Sterile saline in hub of a syringe

See the amastigote!





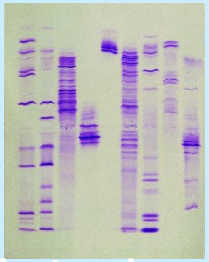
Touch preps

Giemsa staining

Lesion biopsy or aspirate

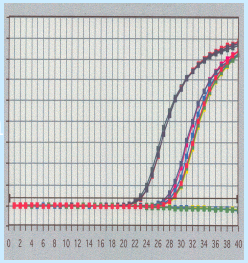
Schneiders, MMI, NNN culture media

Promastigotes in culture



Electrophoresis for speciation

PCR



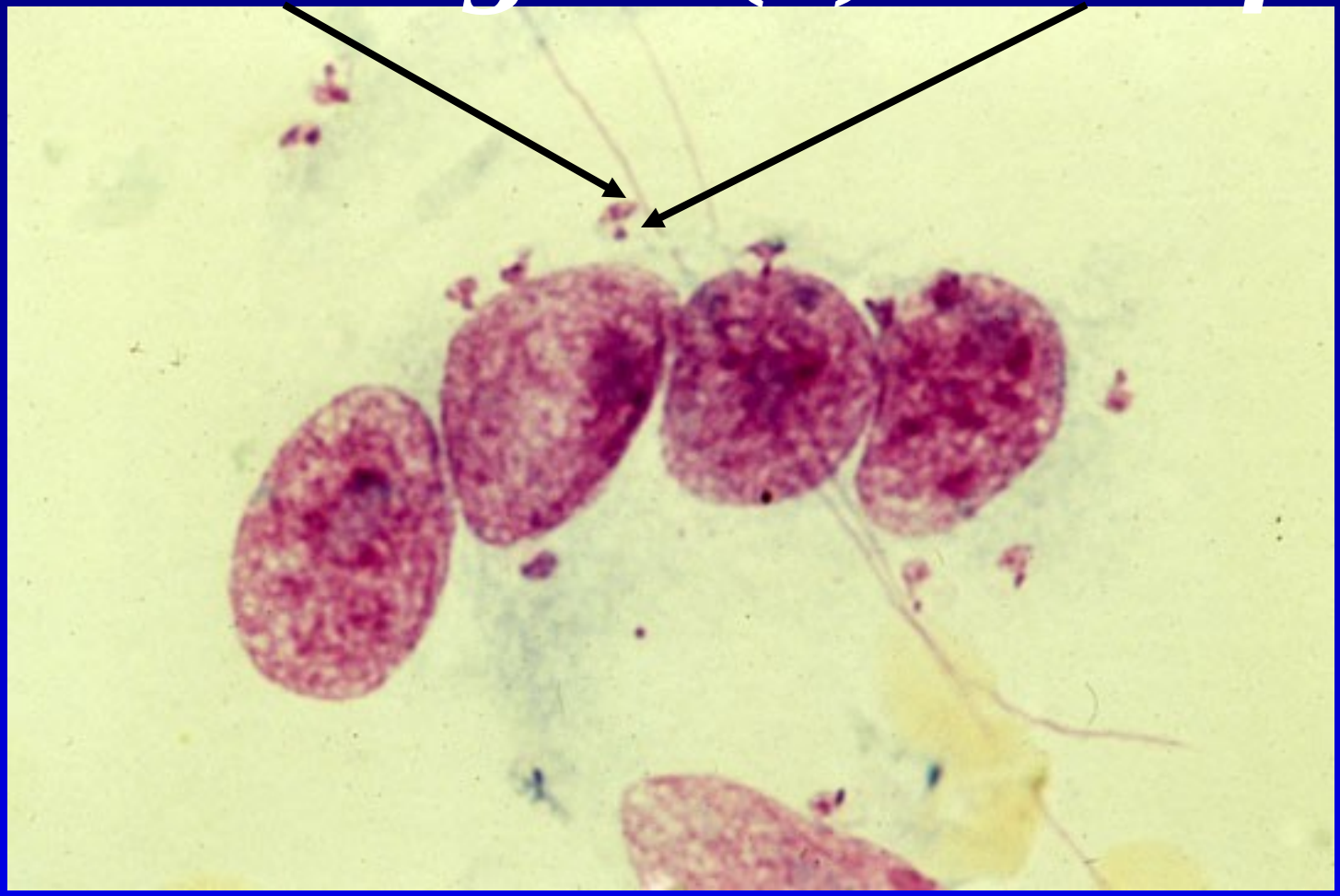
L. major
L. major
L. V. panamensis

Negative control

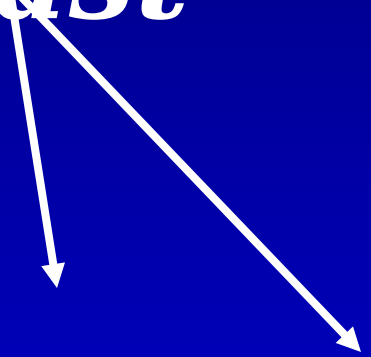
rRNA Probe for Genus Level Identification

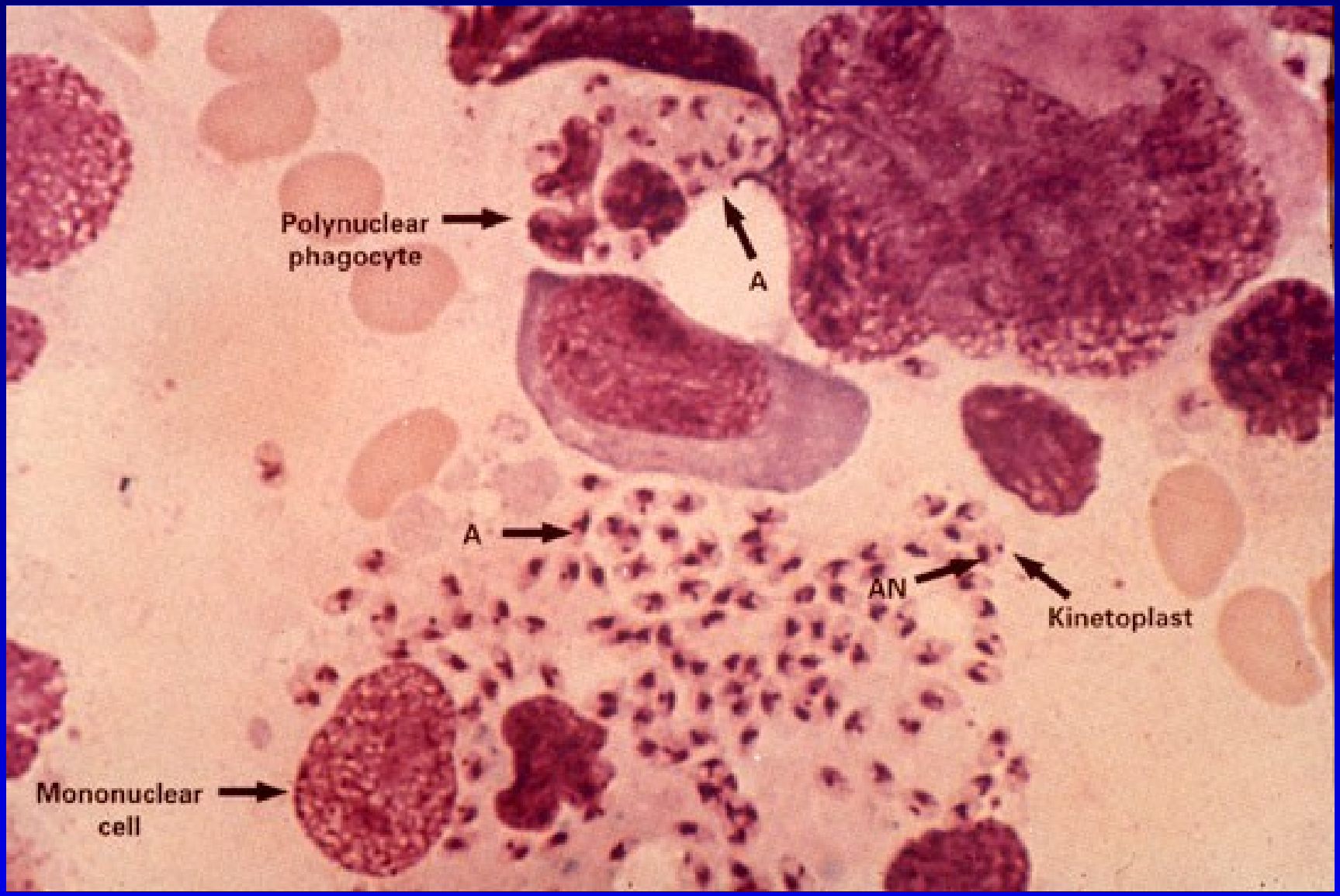
Processing of diagnostic material for Leishmaniasis evaluation

Amastigote(s) Kinetoplast



Kinetoplast



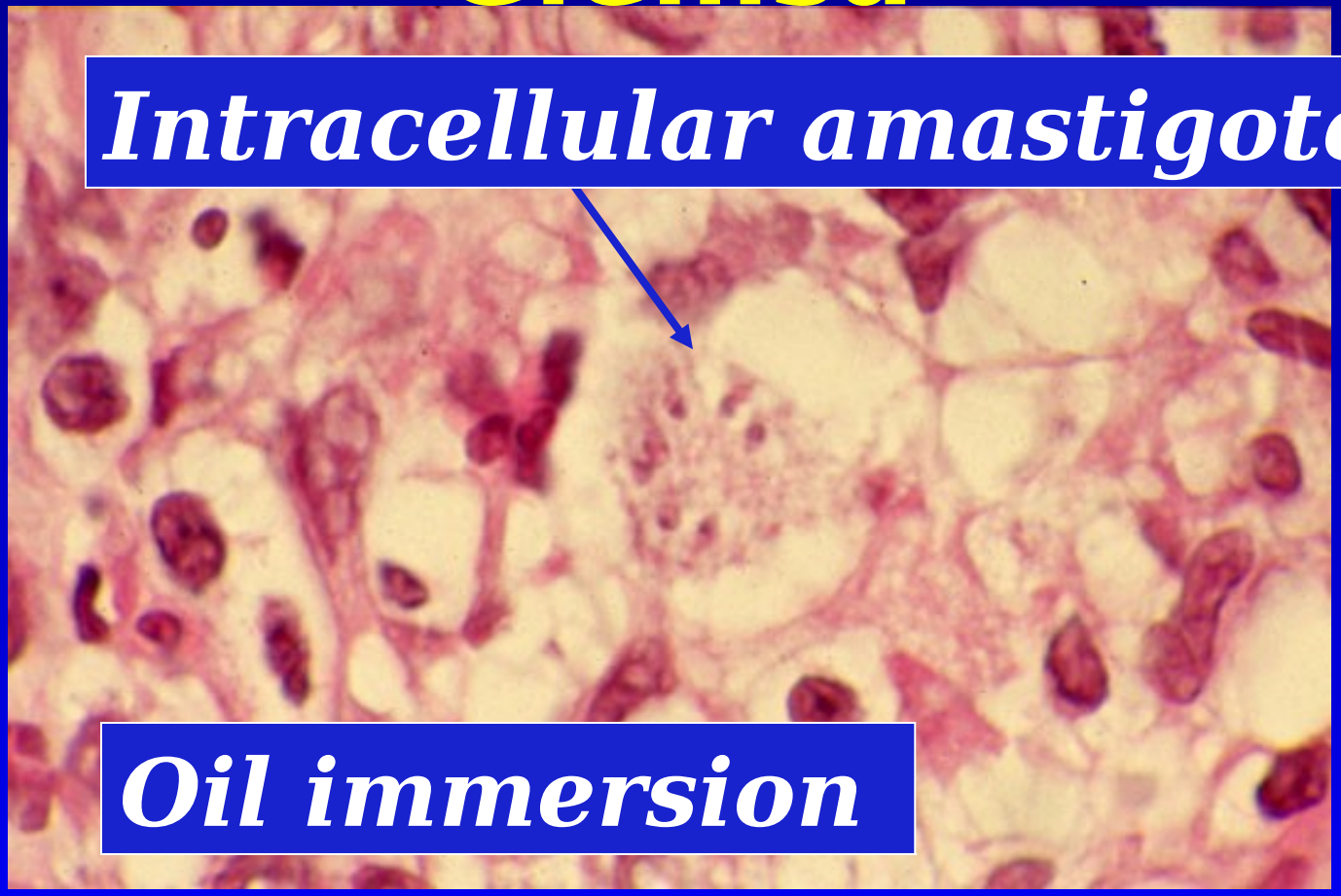


Bone Marrow Aspirate

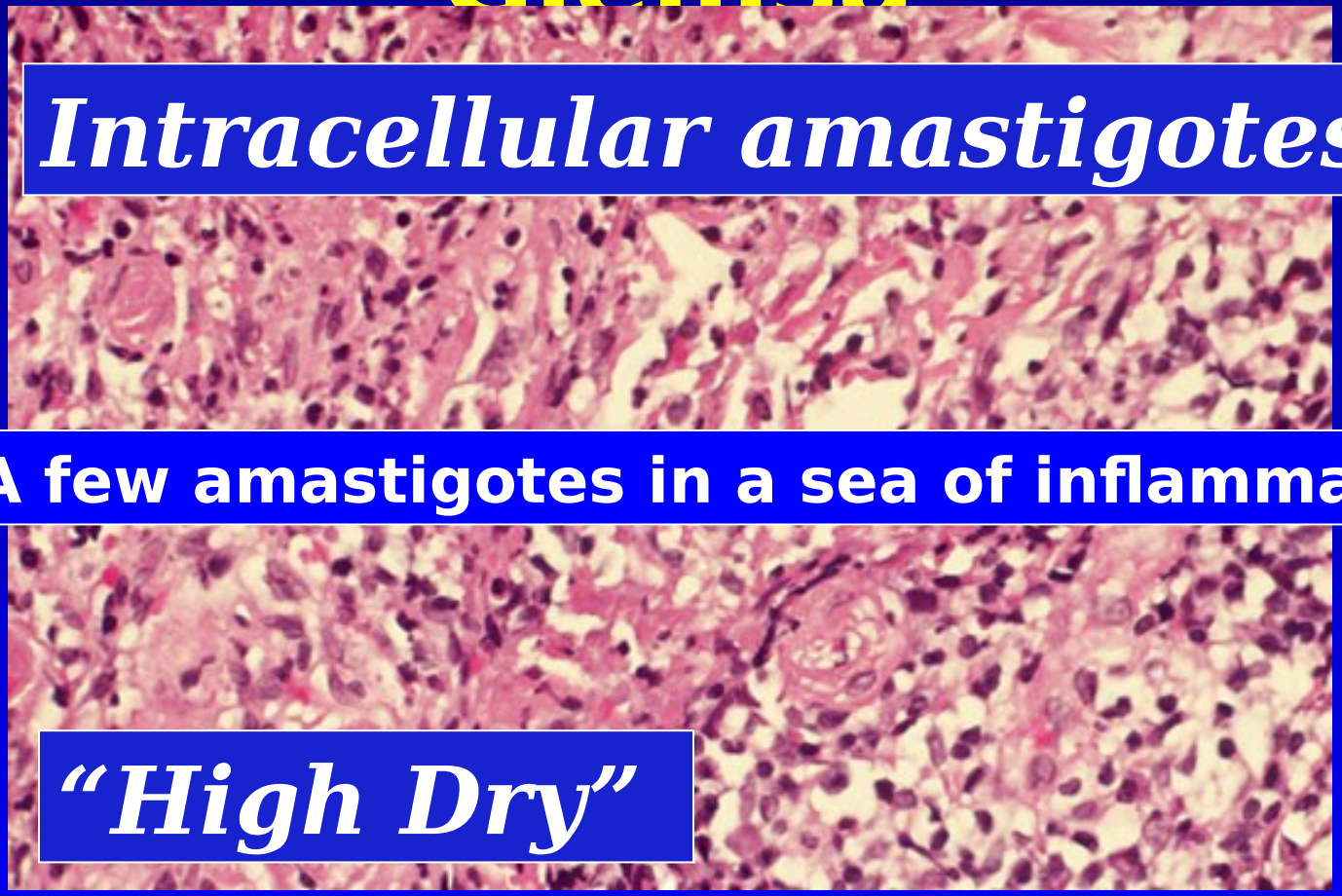
Diff Dx of amastigotes

- "Small dot" disease in macrophages
- No kinetoplast
  - Histoplasmosis - real issue with VL
- (+) kinetoplast
  - Trypanosoma cruzi
    - Cutaneous lesions in post-transplant
  - Leishmania
- **No kinetoplast - no Leish!**

Histopathology: H&E / Giemsa



Histopathology: H&E / Giemsa

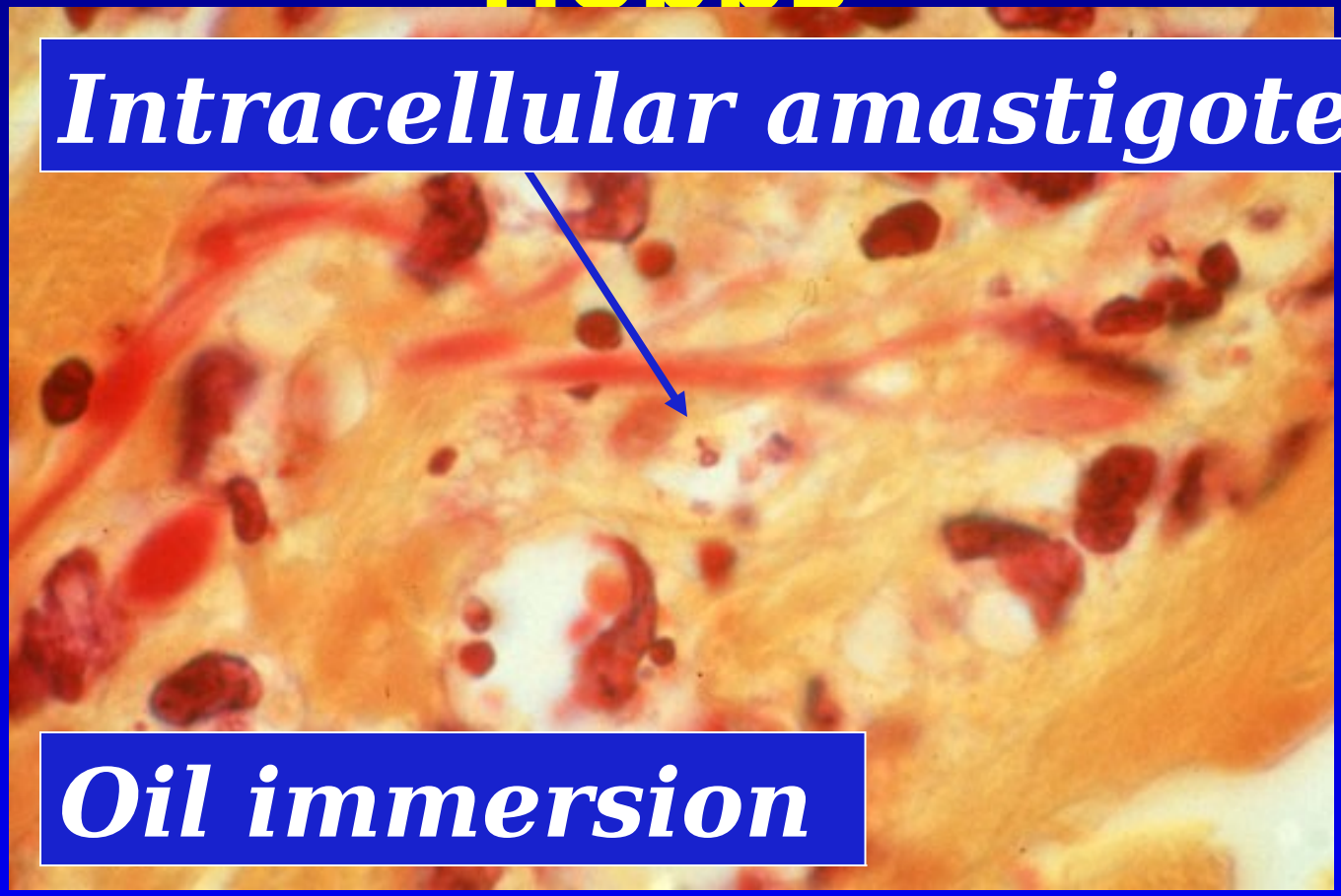


Intracellular amastigotes ?

"A few amastigotes in a sea of inflammatory cel

"High Dry"

Histopathology: Brown & Hopps



Histopathology

- Most North American pathologists do not routinely review slides under oil immersion
- Lack of experience looking for Leish
- Cuts too thick (5-6 µm) vs. 3 µm for Leish
- Review slide for 1 hour under oil to call negative
- Histopathology least sensitive of any method
  - As low as 12% in one study
- Useful to exclude other diagnoses and describe histopathology

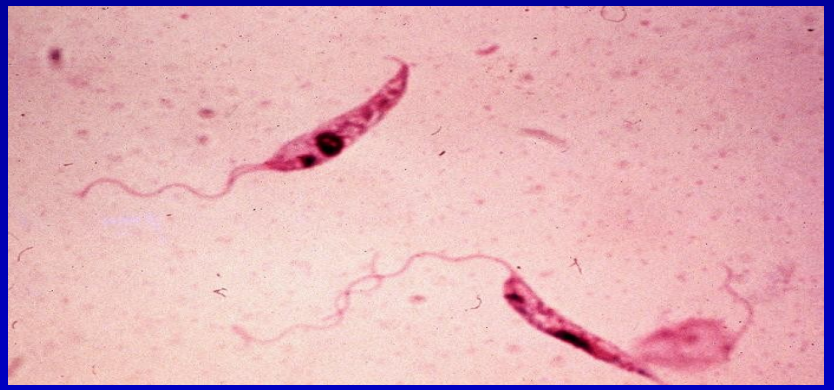
Nodular Presentations

- Slit-skin smears of nodule or nodule margin
- Punch biopsies?
- Not uncommon presentation
  - Part of the natural hx
  - 10% persistent

Culture

- **Complex media / lab skills**
- **Science versus “art”**
- **Asking for the intracellular amastigote to transform into a promastigote and expand**
- **Parasite species growth differences**

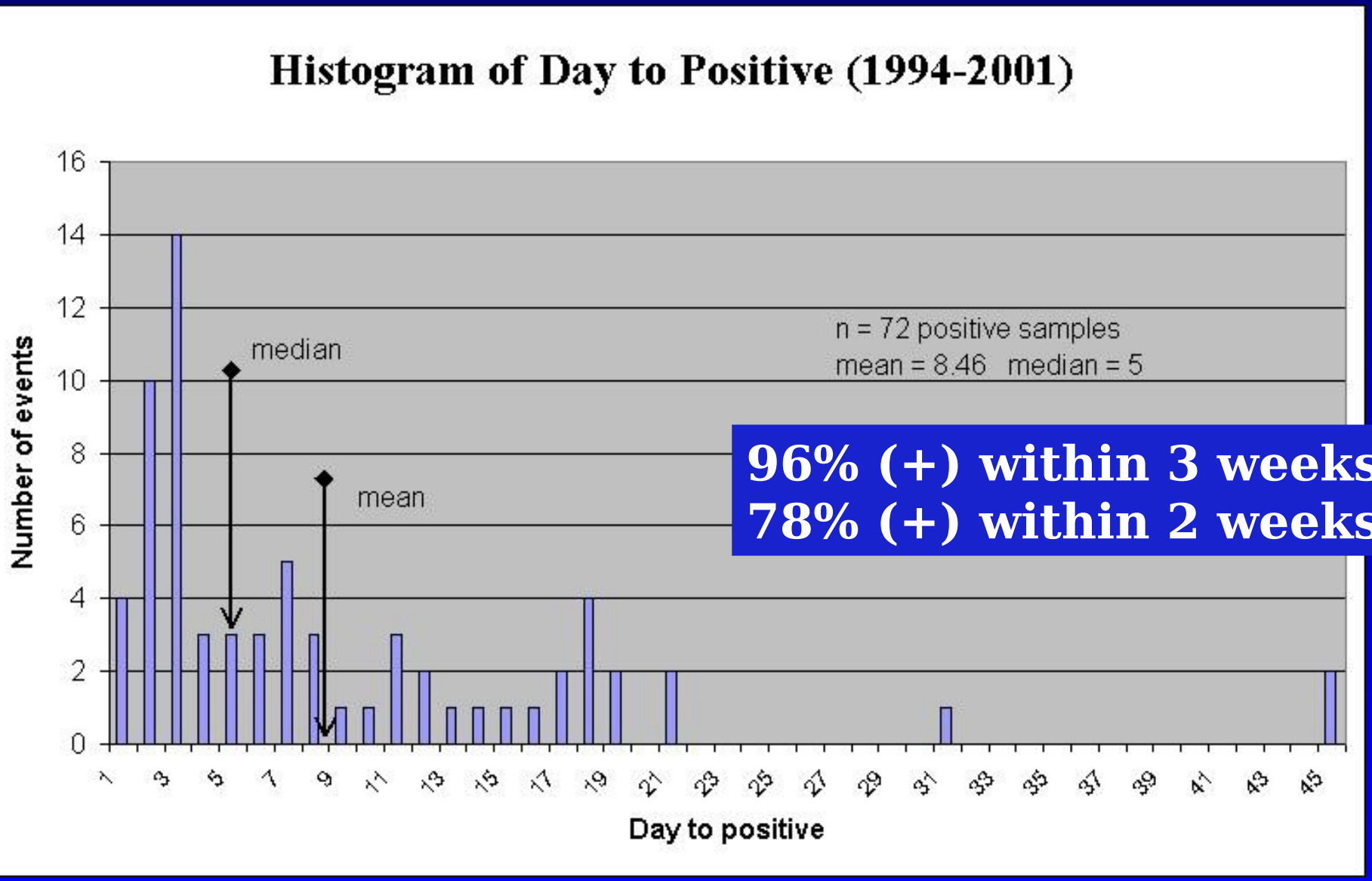
In vitro culture



Association between culture results and concentration of amastigotes on thin smears

Amastigotes / 400 oil immersion fields	Culture results No. positive / total (%)
0	42 / 153 (27)
1-19	36 / 50 (72)
20-199	43 / 53 (81)
200-399	27 / 32 (84)
400-799	42 / 46 (91)
800-1,999	12 / 13 (92)
≥2,000	15 / 15 (100)

Navin TR et al. Am J Trop Med Hyg 1990 42(1),


Histogram of Day to Positive (1994-2001)
Number of events
Day to positive
median
mean
n = 72 positive samples
mean = 8.46 median = 5
96% (+) within 3 weeks
78% (+) within 2 weeks

PCR

- **Genus specific and / or species specific**
- **Sensitivity / specificity with different species, targets, probes, specimens, geographic locations**
- **Who does it?**
- **Where is it done?**

Real-time Fluorogenic PCR for NWCL

- DNA probe specific for conserved region of 16S rRNA
- Paraffin -embedded and fresh human bx tissue
- 100% specific
  - 40 negative controls from multiple other disease states
- 100% sensitive
  - 27 Leish cultures (9 species)
  - 12 paraffin embedded bx
  - 3 fresh human bx

Wortmann G et al. Am J Trop Med Hyg 2001 65(5)

Parasitologic Diagnosis Summary

- **Sample youngest or “most active” lesion(s)**
- **Use more than one technique on more than one sample**
  - **5 smears from dermal scrapings of different sites on the ulcer(s)**
  - **3-5 cultures**
- **Success correlates with parasite burden**
- **Can never exclude the diagnosis with only parasitological methods**

Immunologic Diagnosis

- **Serology (detection of antibodies)**
  - **Not currently useful in CL**
  - **Can be useful in VL**
    - **DAT, ELISA, rK39**
- **DTH - skin testing**
  - **No product available or licensed in the USA**
  - **Useful adjunct in oligoparasitic syndromes such as ML, CL, resolved VL,**

rK39 based serologic tests

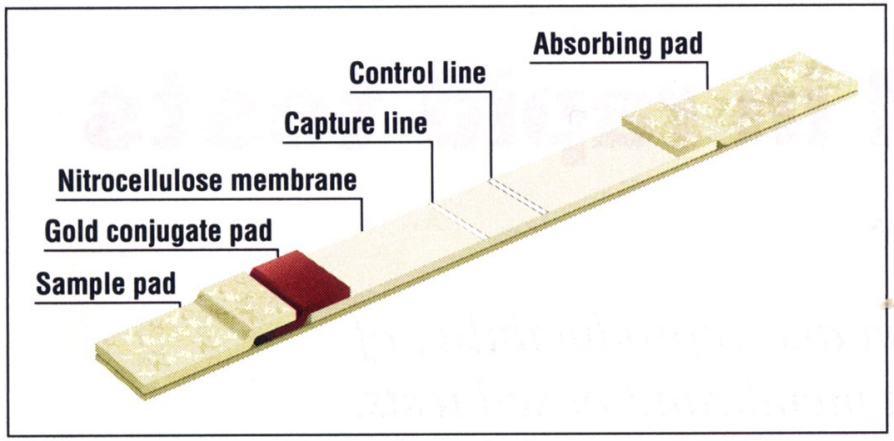


Figure 1. Construction of a lateral-flow rapid test.

- Kalazar Detect™
- FDA cleared via 510K process on 06 May 2003
- InBios International Inc. Seattle, WA
- Detects Ab to rK39 Ag in VL
- > 95 % sensitivity
- Peripheral blood

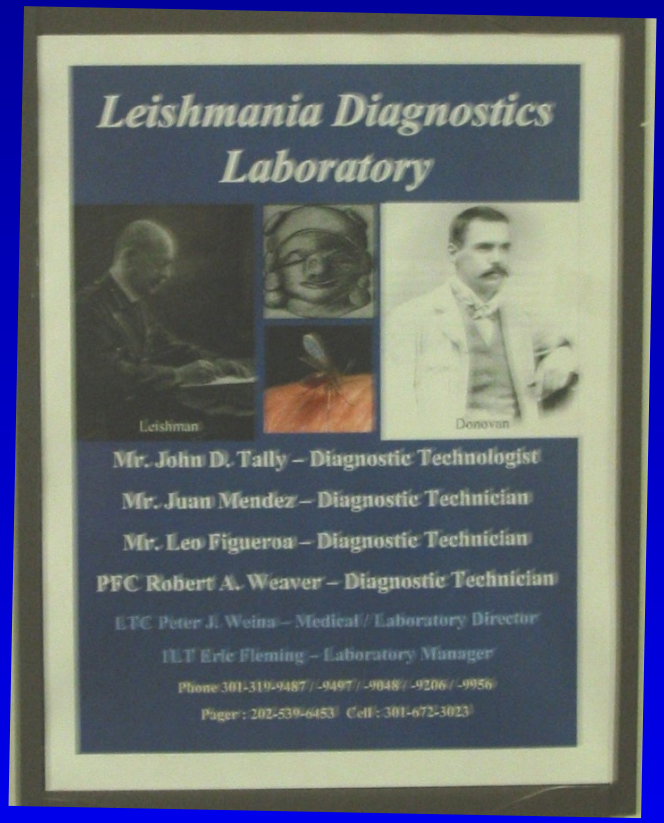
Does it matter what the Leishmania species is?

- Rx or not to Rx?
  - L. braziliensis or L. panamensis
- Choice of drug Rx?
- Duration of Rx?
  - L. major or L. tropica
- Dose?

Species identification

- **Morphology on slide? Not for routine use**
- **Isoenzyme analysis**
  - **Comparison of unknown to reference standards**
  - **Requires cultured promastigotes**
  - **Patients usually treated before result is known**
- **Mab**
- **PCR**

WRAIR Leishmania Diagnostic Laboratory

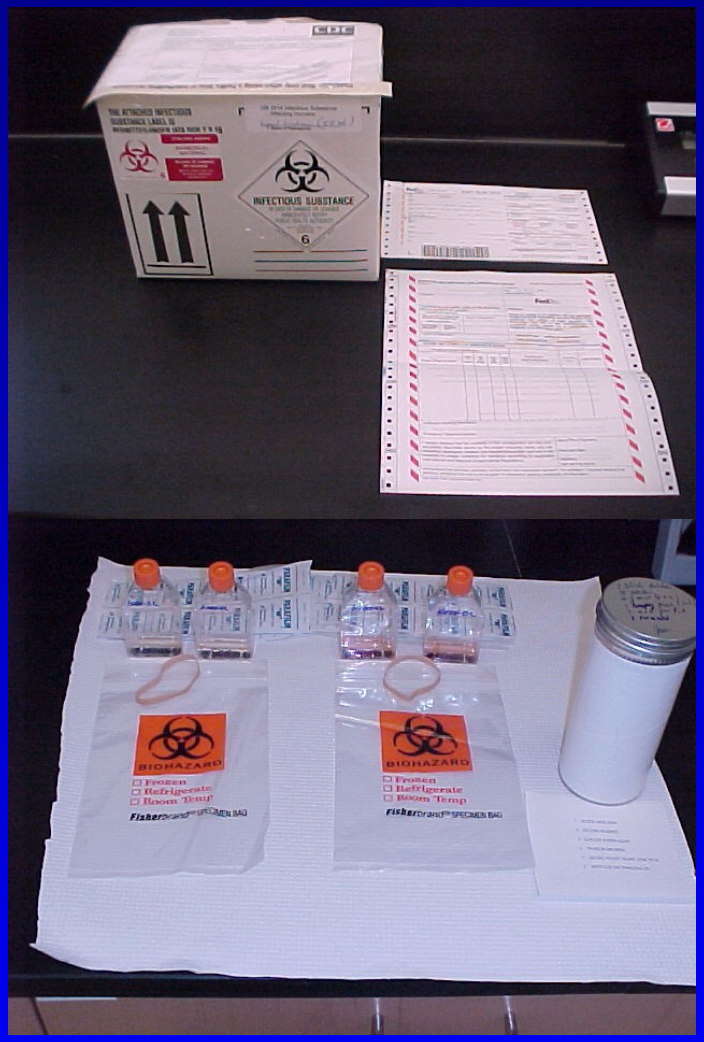

Leishmania Diagnostics Laboratory
Leishman
Donovan
Mr. John D. Tally – Diagnostic Technologist
Mr. Juan Mendez – Diagnostic Technician
Mr. Leo Figueroa – Diagnostic Technician
PFC Robert A. Weaver – Diagnostic Technician
LTC Peter J. Weina – Medical / Laboratory Director
1LT Eric Fleming – Laboratory Manager
Phone 301-319-9487 / -9497 / -9048 / -9206 / -9956
Pager : 202-539-6453 Cell : 301-672-3023

- LTC Peter Weina, Director
- CAP & CLIP certified
- 301-319-9956, 7733, 9497, 9487

WRAIR Capabilities

- Microscopic review of slides
- In vitro culture
- Isoenzyme species identification if culture (+)
- PCR

WRAIR “mail out” diagnostic kit



- Instructions
- Culture media
- Return mailing box with permits
- Vials with EtOH for PCR
- Vials with 10% formalin for histopathology
- Slides, slide holders, punch bx, gauze, etc.

CDC Diagnostic Services

- Frank Steurer, 770-488-4475
- Microscopy
- Culture with isoenzyme analysis
- Serologic testing (IFA)
- No Mab or PCR testing

So how do I treat this?

Amastigotes seen, kinetoplast confirmed

Drug Therapy: Basic Principles

Intracellular parasite

Infection induces relative immunosuppresion

Success of SbV dependent on functional CD4(+) T cells

Poor quality clinical trials

Lack of RDBPC trials

- **Different endpoints**

  Clinical cure = resolution of signs and symptoms of disease

  Parasitolgical cure = eradication of parasites

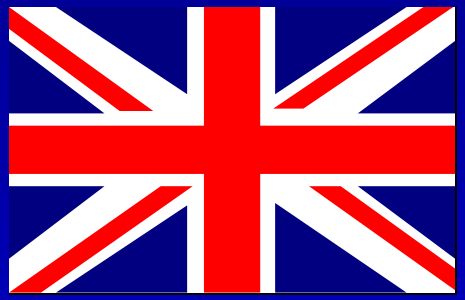
Geographic Variability

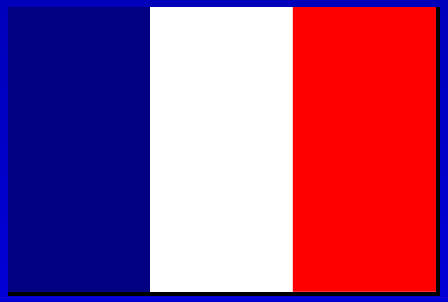
- **Heterogenous populations**
- **Complex disease**

Drug Therapy: Current Status (2003) in USA

- **AmBisome® (Liposomal amphotericin B)**
  - **Approved for Rx of VL by the FDA**
- **Pentostam® [pentavalent antimony, (SbV]**
  - **Available under an IND**
    - **Military personnel - Walter Reed Army Medical Center**
    - **Civilian personnel - CDC**

Drug Therapy: SbV





- **Pentostam® (sodium stibogluconate, Glaxo-Wellcome, UK)**
  - **100 ml bottles at 100 mg Sb / ml**
  - **Traditionally used in Anglophone countries**
- **Glucantime® (meglumine antimoniate, Rhone-Poulenc, France)**
  - **5 ml ampules at 85 mg Sb / ml**
  - **Traditionally used in Francophone, Spanish and Portuguese speaking countries**

20 mg / kg / day X 20 days for LCL
20 mg / kg / day X 28 days for VL and ML

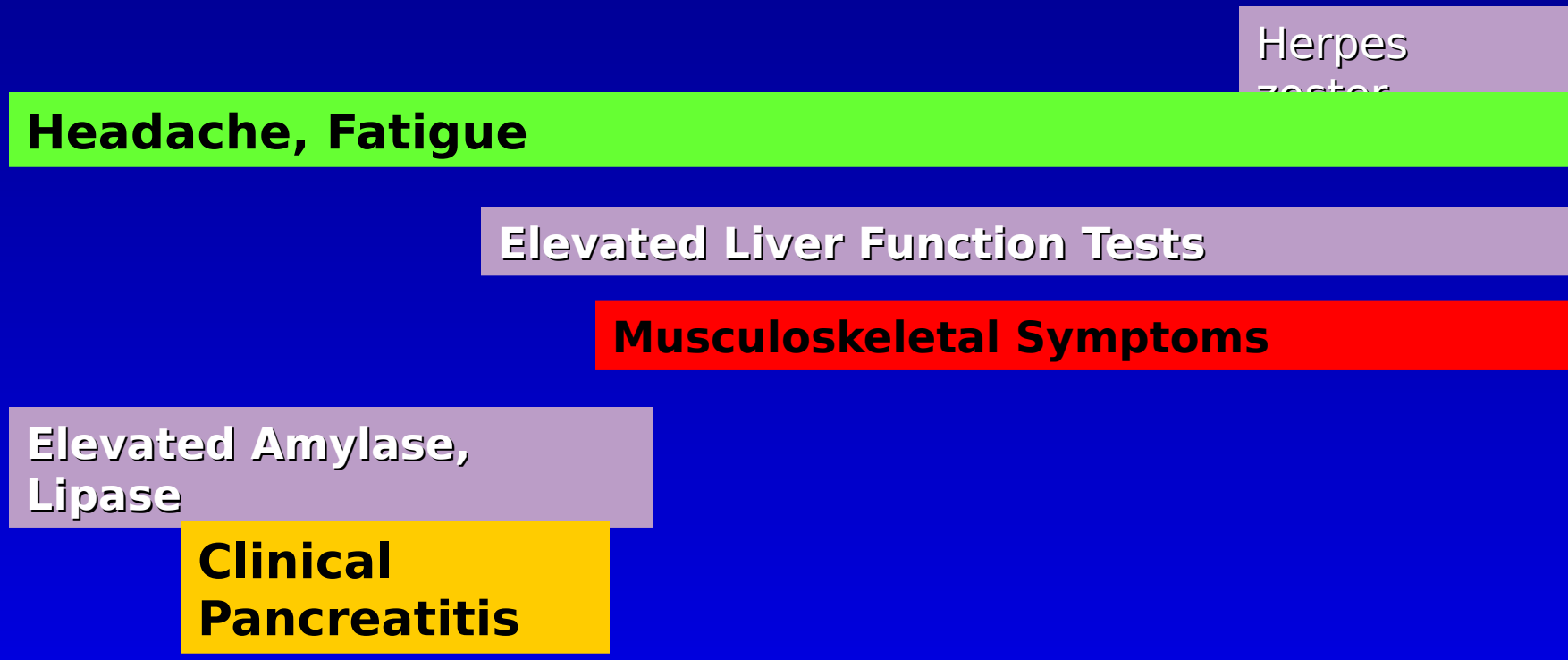
Pentostam®: Side Effects[1]

- **Symptoms:**
  - **Headache, somnolence, fatigue**
  - **Anorexia, nausea, vomiting, abdominal pain**
  - **Large joint arthralgias and stiffness, myalgias**

Pentostam®: Side Effects[2]

- **Signs**
  - **Mid-epigastric tenderness**
  - **Decreased range of motion of large joints**
- **Special Tests**
  - **Increased ALT / AST**
  - **Increased serum lipase / amylase**
  - **Anemia, thrombocytopenia, granulocytopenia**
  - **T wave flattening, nonspecific ST segment changes**
  - **Prolonged QTc interval on ECG**

Sodium stibogluconate:
Timeline for Common Side Effects



Drug Therapy: Current Issues

- **Increasing clinical failures in Indian VL**
  - **Primary drug resistance**
  - **Noncompliance**
  - **Sub-optimal regimens prescribed and used**
- **No effective oral agents for CL, ML**
- **Oral Miltefosine for VL?**

SbV resistance in Bihar, India

- **Map of resistance levels in the Bihar focus of visceral leishmaniasis, India. Orange=high-level resistance, YELLOW=mixed resistance, GREEN=no resistance. Reproduced with permission of Blackwall Publishing from Trop Med Int Health 2002; 7: 293.**

Day 0
Day 7
Day 14
Day 21

6 weeks
after Rx

6 months
after Rx
cm
1
2
3
4

Never attempt surgical excision!

The Epidemiological Triangle

Enzootic Cycle

Sand fl

Mammali Reservoi

Incidental Host

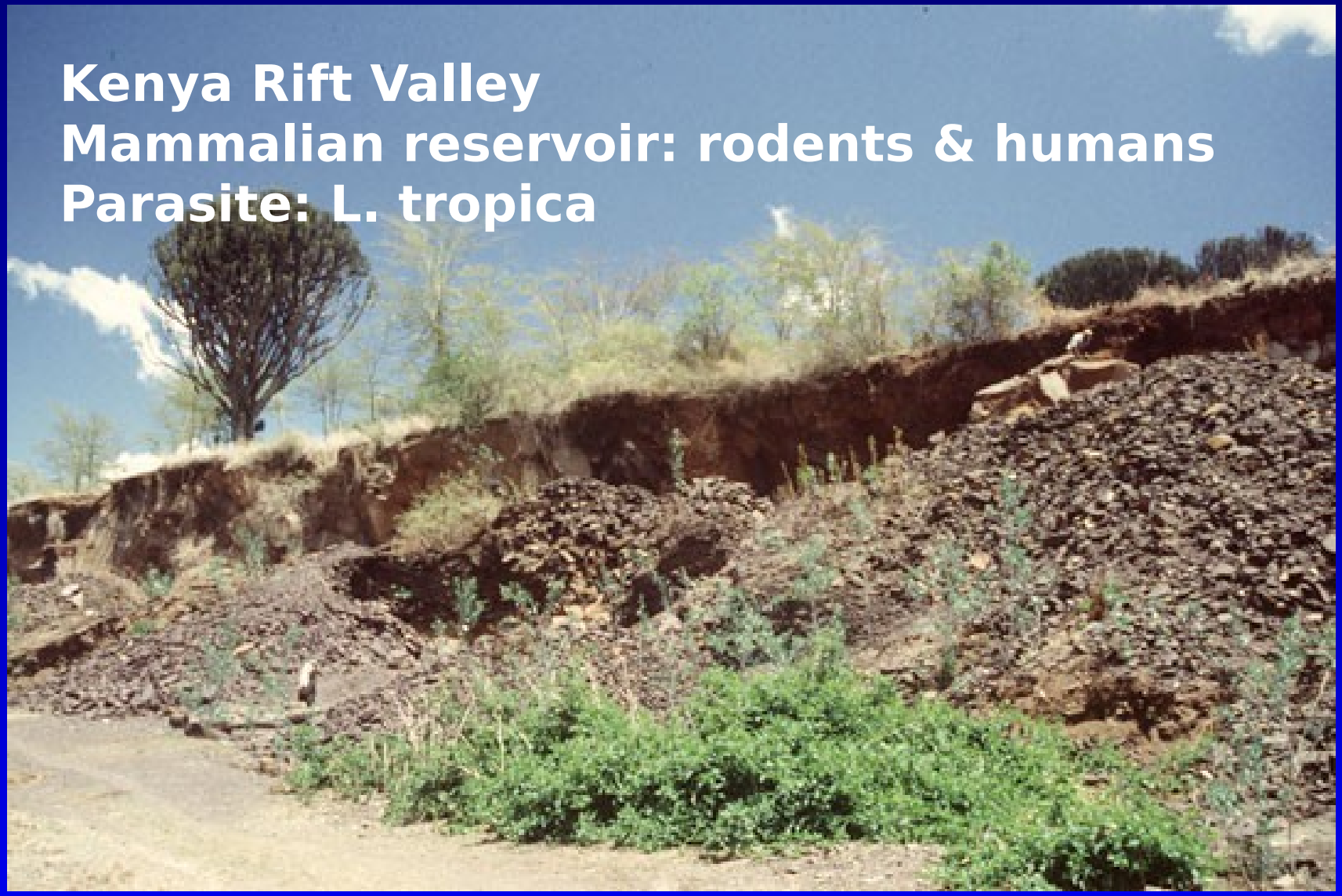
Man and his Activities

Modes of Transmission

- **Sand fly insect vector**
- **Parenteral**
  - **Blood transfusion**
  - **Intravenous Drug Abuse (needle sharing)**
- **Congential**
- **Occupational (laboratory needle stick)**
- **Sexual**
- **Person to person?**

Amazon Rainforest
Mammalian reservoir: rodents
Parasite: L. braziliensis

Brazilian peri-urban
Mammalian reservoir: domestic dogs
Parasite: L. chagasi


Kenya Rift Valley
Mammalian reservoir: rodents & humans
Parasite: L. tropica

Gangetic plains, Bihar, India
Mammalian reservoir: humans
Parasite: L. donovani

Leishmaniasis as a Military Threat[1]

- **WWII - Karum river valley (Iraq)**
  - **630 cases of CL in US forces in 3 months**
- **1967 - Israeli Defense Force near Jericho**
  - **Scores of cases, 50% attack rate**
- **1984 – Puerto Rican NG at JOTC, Panama**
  - **14 / 64 (22%) cases of CL**
- **1986 – 484 cases in Guatemalan Army**
  - **1-2% of force, morale problem**

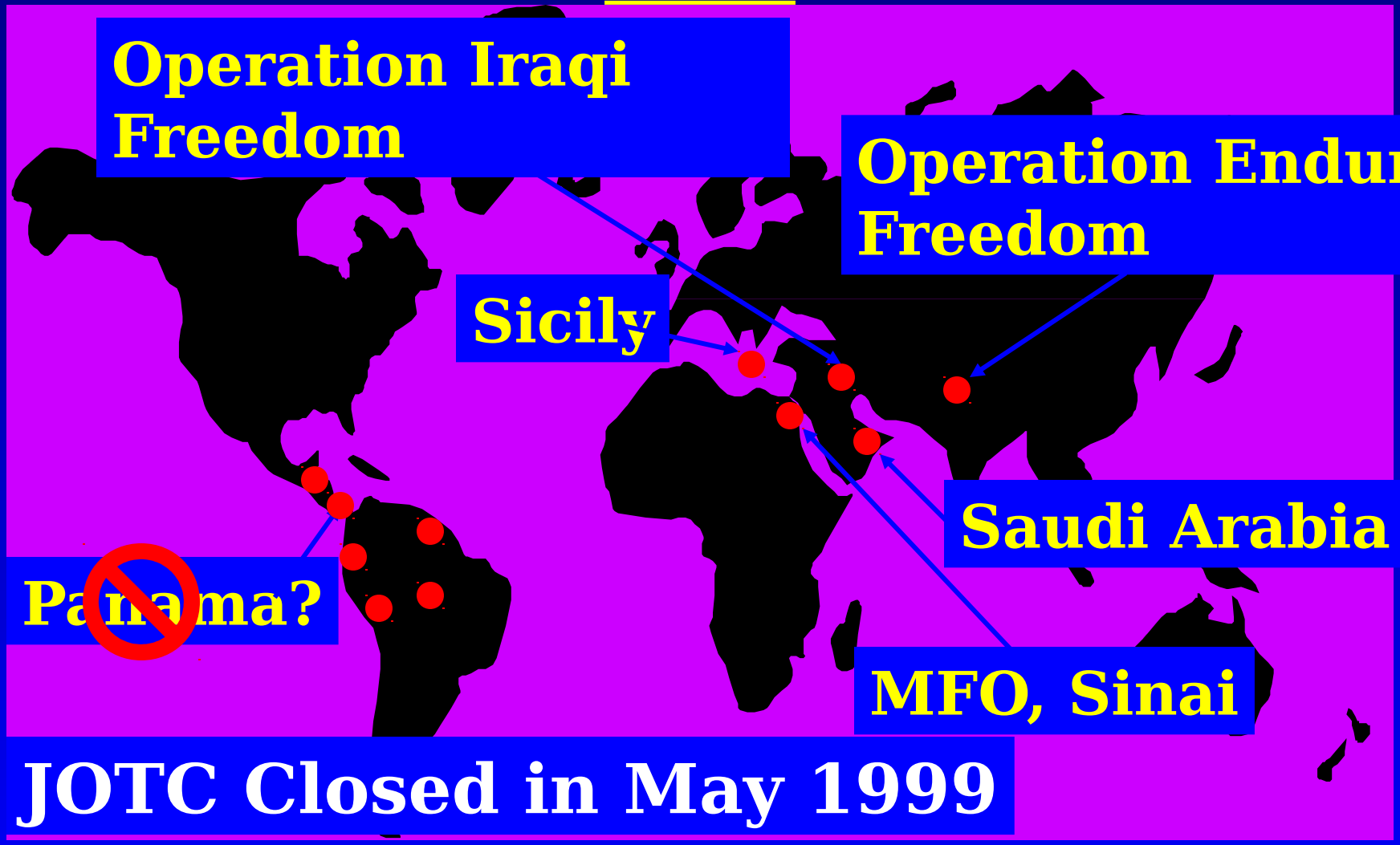
Leishmaniasis as a Military Threat[2]

- **1990 - Multinational force in the Sinai**
  - **113 cases of CL per 1,000 peace keepers**
- **1990 – Canadian paratroopers in Guyana**
  - **17 / 27 (63%) cases of CL in 6 hours!**
- **1992 – Colombian Army**
  - **3,000 cases of CL reported**
- **1992 - Jungle training in French Guiana**
  - **6 / 12 (50%) cases of CL in USMC in 2 weeks**

Leishmaniasis as a Military Threat[3]

- **1992 - ODS**
  - **12 cases of viscerotropic leishmaniasis caused by *L. tropica***
  - **20 cases of CL**
- **1980s to present**
  - **Thousands of cases of CL in Iranian and Iraqi forces during border war**
  - **Both sides routinely vaccinated troops**

Leishmaniasis Risk for US Military for 2003



NAS Sigonella

Leishmaniasis in Sicily

- **Naval Air Station Sigonella is located in Catania province, Sicily, an active focus of human VL**
- **30 - 40 cases of human VL per year in Italian hospitals since 1995.**
- **4 cases in US military dependent children since 1996**
- **Unknown number of “sub-clinical” infections**

Canine Leishmaniasis in Sicily

- Clinical and serologic testing of 50 companion dogs belonging to US military personnel
- 60% had increased antibody titers
- Inapparent infection in dogs is common
- Known sand fly vectors trapped in study area

Canine visceral leishmaniasis in Sicil
Mil Med 2000 Jan; 165(1): 29-32.

Afghanistan

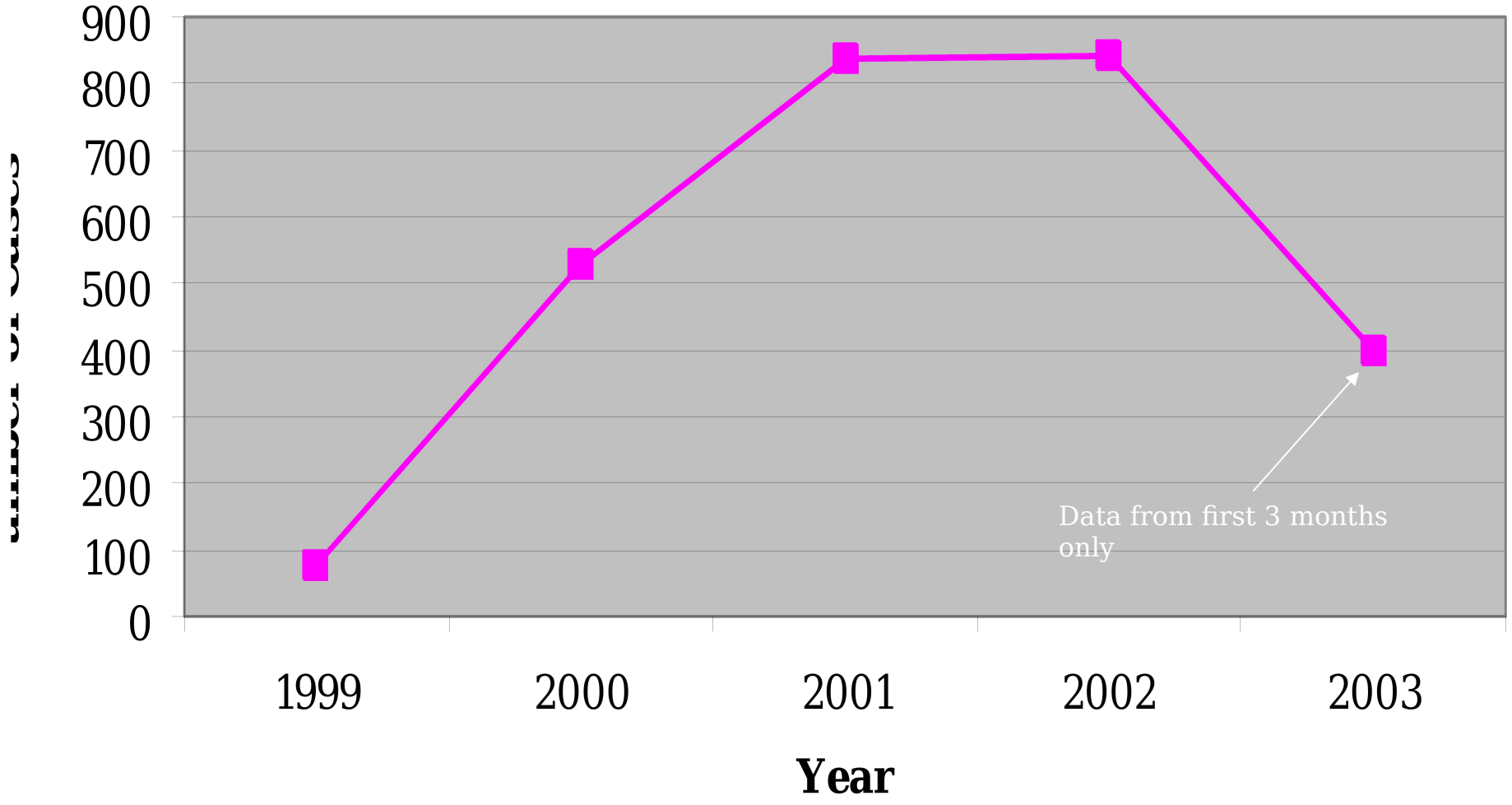
- Epidemic *L. tropica*
- Kabul and elsewhere
- Reservoir = Man, ? dog
- *P. sergenti* is vector
- ?? Risk for deployed troops

US Army special forces soldier
Presents to ‘TMC” in Bagram, Afghanistan
@ 3 week history of expanding ulcer on bac
1+ tender, not pruritic
What do you do??

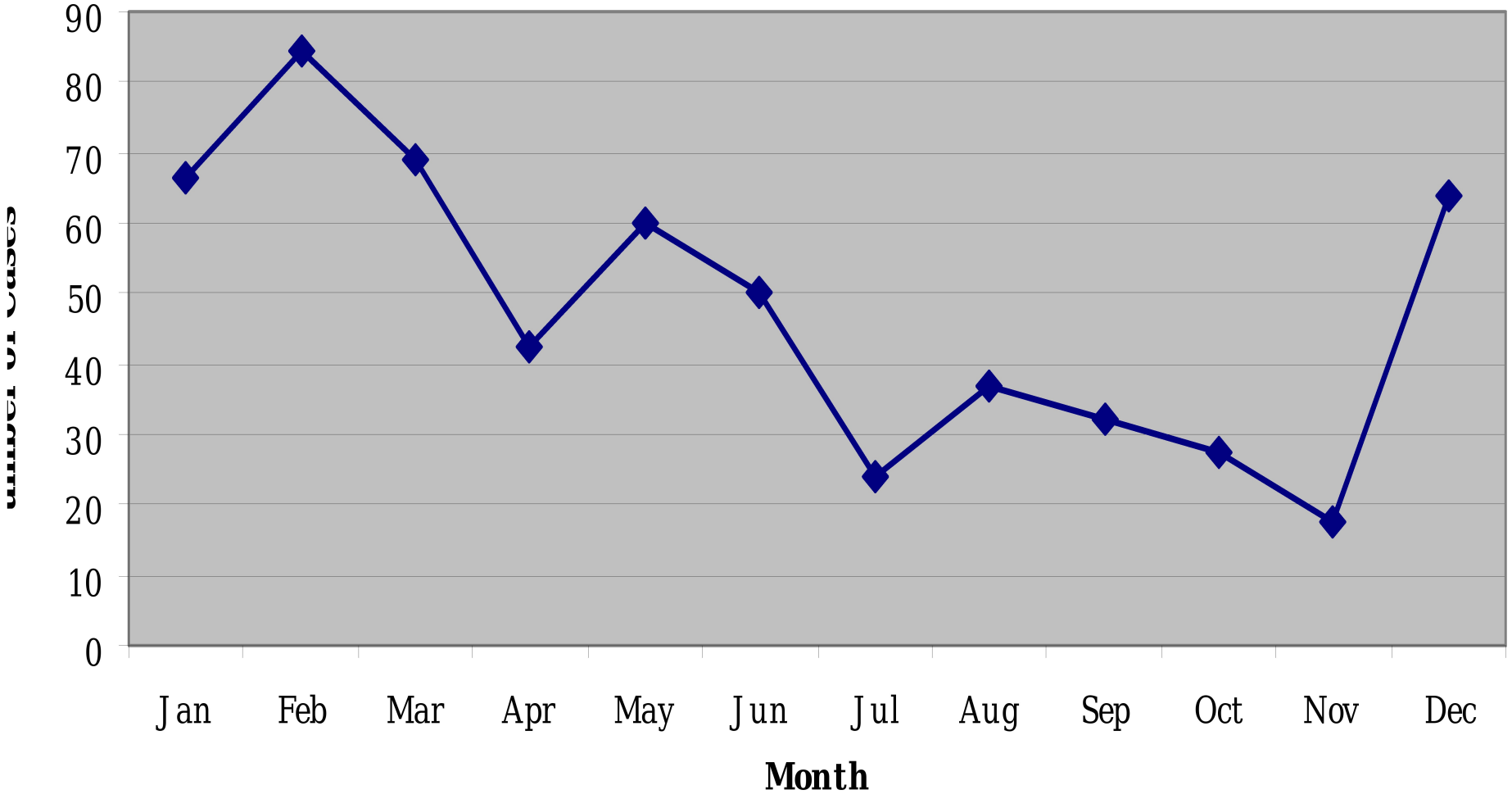
Iraq: Operation Iraqi Freedom

Talil air base
Ramadi
Habbaniyah
BAGHDAD
Al Fallujah
Salman Pak
Khorramabad
Badrah
Al Mahmudiyah
Al 'Azizlyah
As Suwayrah
Al Musayyib
Karbala'
Al Hillah
Al Hindiyah
Al Kut
'Ali al Gharbi
Dezful
Al Hashimiyah
Al Hayy
Al Kufah
An Najaf
Atak
Al Kumayt
Nukhayb
Ad Diwaniyah
Qal'at Sukkar
Abu Sukhayr
Ash Shamiyah
Al 'Amarah
Ar Rifa'i
Qal'at Salih
Ash Shinafiyah
Al Ramaythah
Ash Shatrah
Ash Samawah
Euphrates
An Nasiriyah
Al Qurnah
Ar'ar
Al Kaba'ish
Suq ash Shuyukh
Hawr al Hammar
Al Basrah
Khorramshahr
Abadan
As Salman
Az Zubayr
Umm Qasr
Al Busayyah
Al Faw
Jazirat Bubiyan
Rafha
Al Jahrah
KUWAIT
Hawalli
SOUTH
WESTERN
ASH SHAMIYAH DESERT
KUWAIT
UDI ARABIA

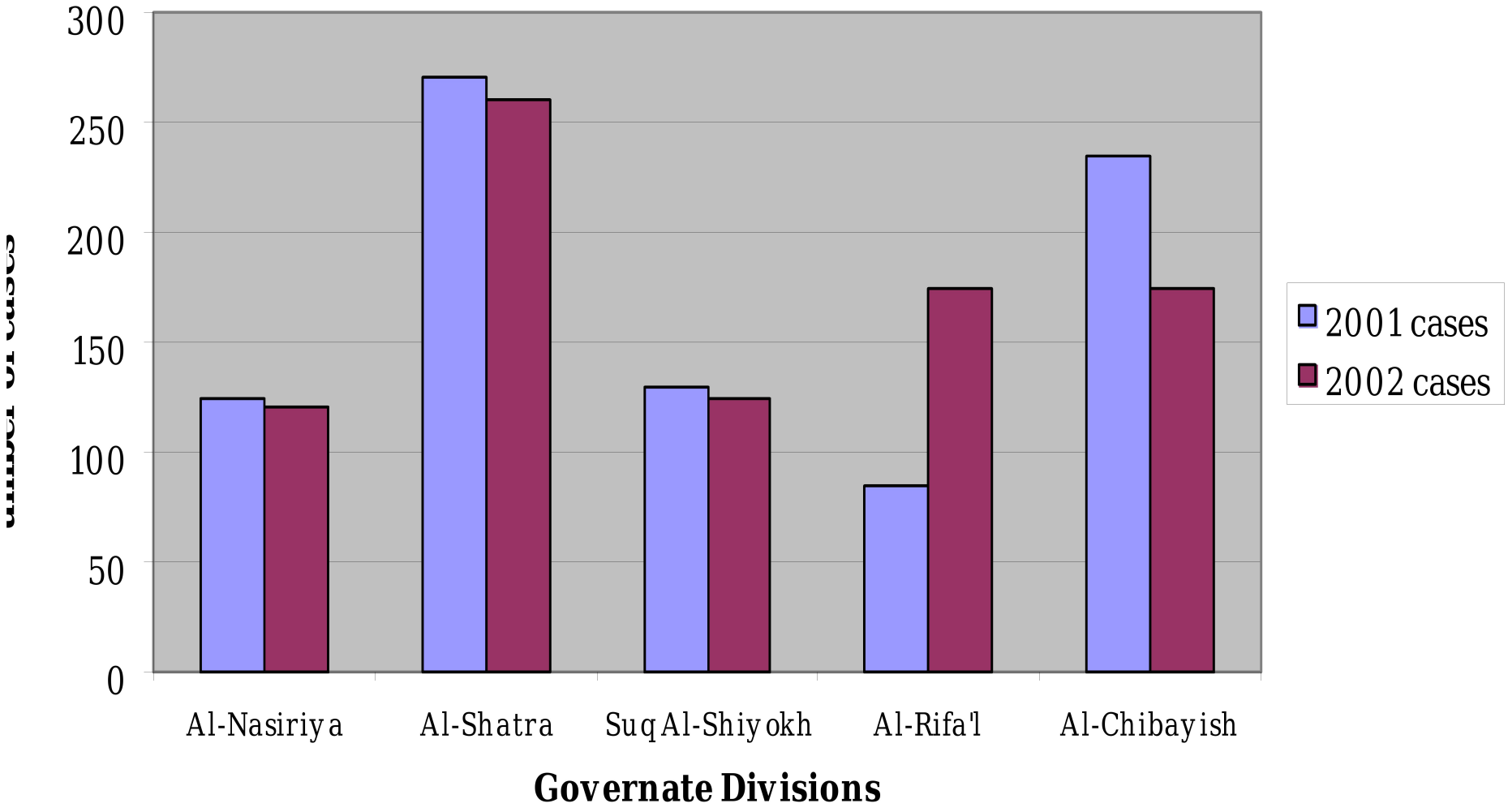
Clinical Visceral Leishmania
Thi-Qar Governate, Iraq

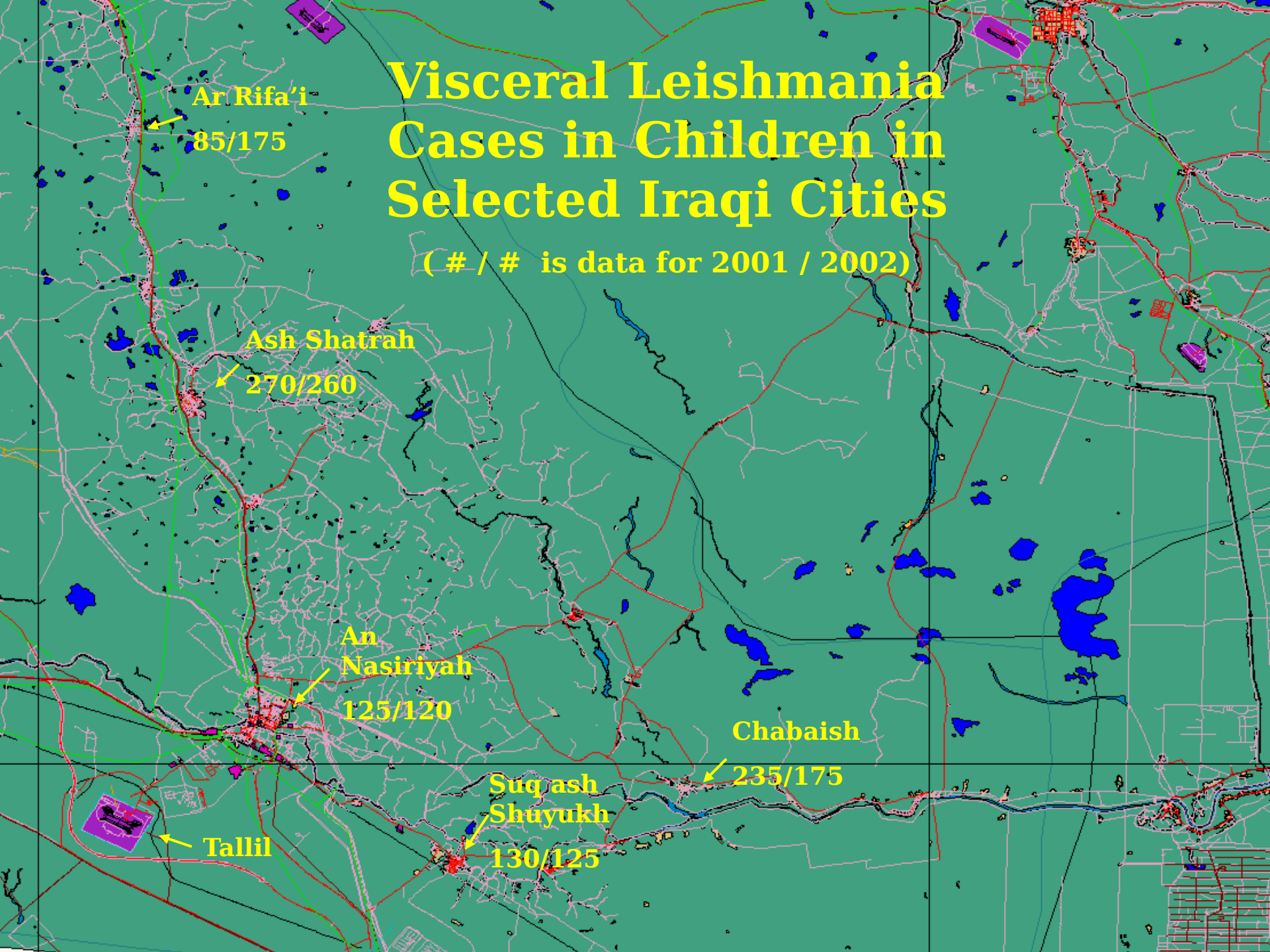


Mean number of Visceral Leishmania Cases Thi-Qar Governate, Iraq (1999-2002)



Distribution of Visceral Leishmania Thi-Qar Governate, Iraq




Visceral Leishmania Cases in Children in Selected Iraqi Cities
(# / # is data for 2001 / 2002)
Ar Rifa'i
85/175
Ash Shatrah
270/260
An Nasiriyah
125/120
Chabaish
235/175
Suq ash Shuyukh
130/125
Tallil

Current Leishmaniasis Treatment in US Military Personnel

- **WRAMC is a DoD Leishmaniasis treatment Center for Excellence**
- **200+ patients diagnosed at the WRAMC to date**
- **All cutaneous leishmaniasis**
  - **3 Operation Enduring Freedom (Afghanistan)**
    - **L. topica**
  - **>200 from Operation Iraqi Freedom**
    - **L. major**
- **None diagnosed with visceral leishmaniasis**

OCT 16 2003

Treatment Options For Cutaneous Leishmaniasis caused by L. major

- No Treatment
- Local (physical) Therapies
  - ThermoMed
- Topical medications: paromomycin
- Oral medications: fluconazole
- IV medications: amphotericin B deoxycholate
- IV pentavalent antimony: sodium stibogluconate (Pentostam®)

Heat Treatment

- ThermoMed device
- Being used at WRAMC

Treatment Options

- **Sodium stibogluconate (Pentostam®)**
  - **Treatment IND**
  - **IND held by Surgeon General of the Army**
  - **WRAMC currently only DoD site with protocol (since 1978)**
  - **20 days of IV therapy [20mg/kg/d]**
    - **10 days for *L. major* (with an investigator option for 20 days for facial, large or slow to heal lesions)**
  - **Obtained from Glaxo Smith Kline (Great Britain)**
  - **Patients treated as outpatients**

Current Pentostam Experience (n=79)

- **85% (67/79) myalgias/arthralgias**
  - **19% (15/79) requiring change in therapy**
  - **Recent change to 10 day course of therapy may improve this side-effect**
- **2 patients with urticaria/angioedema**
- **22% (17/79) did not complete full course of therapy**

Data from Dr. G Wortmann

Results

Results

Prevention

- **Avoidance of sand fly vector**
- **Individual Measures**
- **Unit measures**

Avoidance

- **Microhabitats lead to focal areas of high risk**
- **Sand flies are evening and night time biters**
- **Sandflies are poor fliers**
  - **Windy areas**
  - **No vegetation**

Barriers

- **PPMs!**
  - **Proper uniform and use**
  - **DEET repellants**
  - **Use of bednets**
  - **Permethrin impregnated clothing and bed nets**

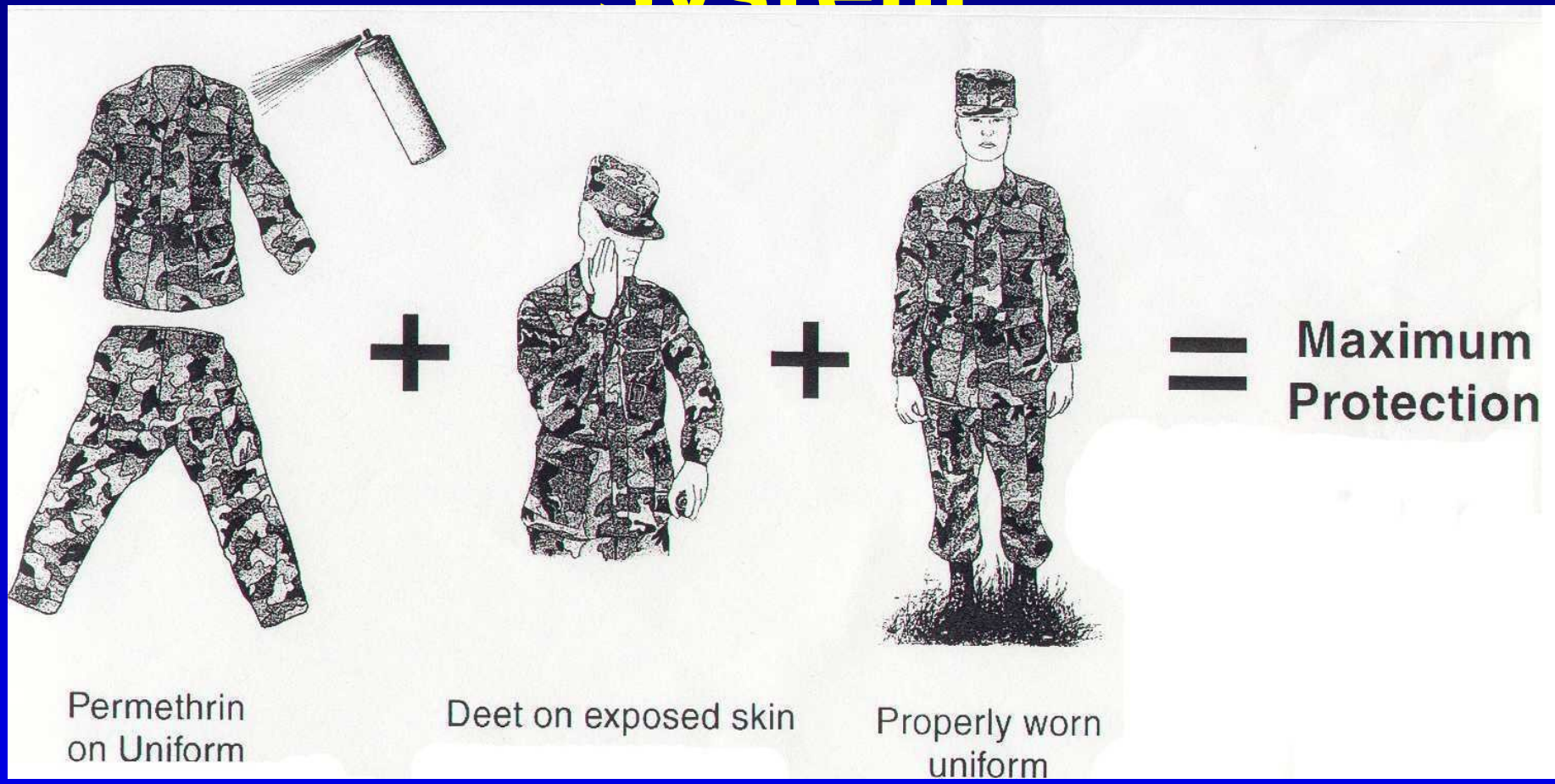
Unit Measures

- Cleared compounds
- Rodent control
- Area or barrier insecticide use
- Education of the soldier and chain of command
- Use of a “knowledge card”

3M
ULTRATHON
INSECT
REPELLENT
2 FL. OZ. • 59 ml

PERMANONE
TICK REPELLENT
REPELS & KILLS
MOSQUITOES, TICKS
& CHIGGERS
CLOTHING TREATMENT ONLY
DO NOT APPLY TO SKIN
KEEP OUT OF REACH OF CHILDREN
CAUTION

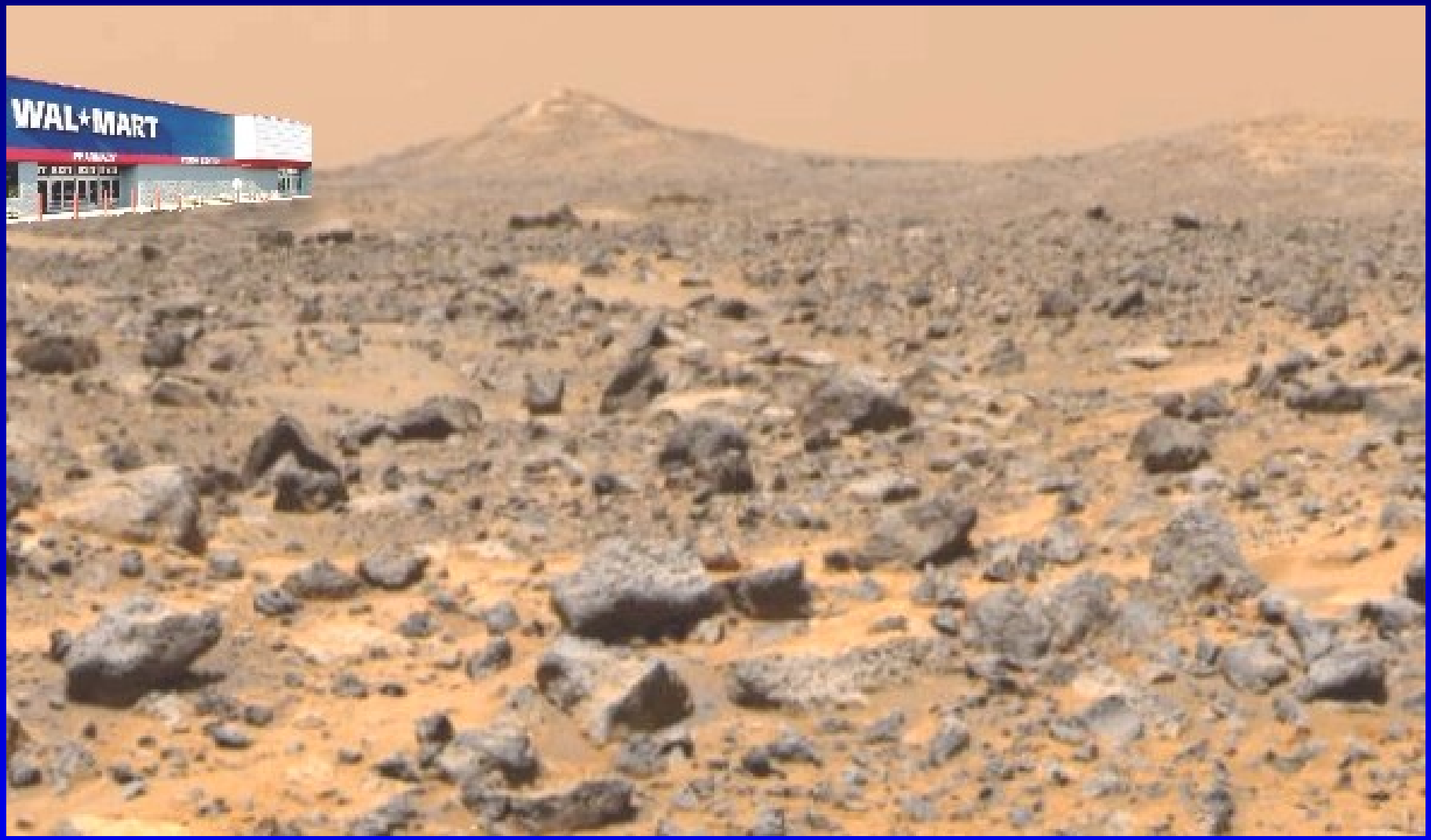
DoD Insect Repellent System



NSN 6840-01-278-1336
Permethrin Spray Can

NSN 6840-01-284-3982
DEET lotion

NSN 6840-01-345-0237
IDA Impregnation Kit


WAL*MART

Any questions or consultation

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